
Specify
LHC

BRITISH SURGICAL PRACTICE

SURGICAL PROGRESS
1953

Under the General Editorship of
SIR ERNEST ROCK CARLING, LL.D., F.R.C.S., F.R.C.P., F.F.R.
CONSULTING SURGEON, WESTMINSTER HOSPITAL

and

SIR JAMES PATERSON ROSS, K.C.V.O., M.S., F.R.C.S.
SURGEON AND DIRECTOR OF SURGICAL
CLINICAL UNIT, ST. BARTHOLOMEW'S HOSPITAL;
PROFESSOR OF SURGERY, UNIVERSITY OF LONDON

BUTTERWORTH & CO. (PUBLISHERS), LTD.
LONDON

AFRICA	BUTTERWORTH & CO. (AFRICA), LTD. DURBAN: GOODRICKE'S BUILDINGS, MASONIC GROVE	
AUSTRALIA:	BUTTERWORTH & CO. (AUSTRALIA), LTD SYDNEY: 8 O'CONNELL STREET MELBOURNE: 430 BOURKE STREET BRISBANE: 240 QUEEN STREET	
CANADA:	BUTTERWORTH & CO. (CANADA), LTD. TORONTO: 1367 DANFORTH AVENUE	
NEW ZEALAND	BUTTERWORTH & CO. (AUSTRALIA), LTD. WELLINGTON: 49/51 BALLANCE STREET AUCKLAND: 35 HIGH STREET	

PRINTED AND BOUND IN ENGLAND BY
HAZELL WATSON AND VINEY LTD
AYLESBURY AND LONDON

PUBLISHERS' ANNOUNCEMENT

Surgical Progress for 1953 is the third of an annual series of supplementary volumes to *British Surgical Practice*. It is designed to keep the eight main volumes up to date in an ever-increasing field of surgical knowledge. This is being done in three ways—by original articles, critical surveys and abstracts.

Subscribers to the main work will find reference to this supplementary volume much facilitated by the provision of a "Noter-up" section, and a correct understanding of the method of its use will considerably enhance the value of both the main work and *Surgical Progress* It will, moreover, save a great deal of time.

Non-subscribers will find the "Noter-up" section of value in that it is alphabetically arranged and gives at a glance information as to the presence or absence of recent material on any particular subject. Consequently, the book can be used independently.

Every article in the main volumes of *British Surgical Practice* has a Key Number, which appears at the commencement of each article and also at the top left-hand corner of every right-hand page. In order to ascertain whether there has been any recent advance in the particular subject to which reference is being made, the reader should merely turn to the appropriate Key Number which appears in the left-hand margin of the "Noter-up" section. He will there find either a note that no further references appear or information as to the type of new matter incorporated by way of article, survey or abstract. This is amplified by a brief outline of the content of the recent addition

Subscribers who turn direct to the abstract section will find that there also the keyed arrangement has been followed.

BUTTERWORTH & CO (PUBLISHERS) LTD.

September, 1953

CONTENTS

PART I—ORIGINAL ARTICLES

CONTENTS

PART I—ORIGINAL ARTICLES

PART II—CRITICAL SURVEYS

PART III—ABSTRACTS

NOTER-UP, 1953

INDEX

INTRODUCTION

In compiling this volume of *Surgical Progress* for 1953 we have continued to follow our policy of making good the omissions in *British Surgical Practice*, of bringing certain articles up to date, and of introducing as entirely new matter articles on recent developments in surgery which appear to us to be substantial and likely to be permanent contributions to surgical science or technique.

In the first category there are the articles by Mr. Allison on Cardiospasm and by Mr. Holdsworth on Fractures of the Pelvis, both important subjects which were left out of consideration in the original work. In the second we have contributions from Messrs. Lloyd-Davies, Naunton Morgan, and Goligher on the Surgery of the Colon; from Professor Milnes Walker on Portal Hypertension; from Mr. Rycroft on Corneal Grafting; from Mr. Wilkinson on Fluid and Electrolyte Balance; from Mr. Tubbs on Constrictive Pericarditis; and from Mr. Black on Detachment of the Retina. All of these articles will be found to be of great value as addenda to *British Surgical Practice*, since they incorporate advances which have occurred since the original articles on these subjects were written.

The remaining articles deal with subjects which have become established in surgical practice since our original work was published, and are in that sense recent advances in surgery. They include the articles by Sir James Learmonth and Dr. Richard Turner on The Syndrome of the Carotid Sinus; by Professor Rob and Mr. Eastcott on Arterial Grafting; by Mr. Richard Johnson on the Surgical Aspects of Meningitis; by Mr. Holmes Sellors on Biological Decortication; by Professor Haddow on the Chemotherapy of Malignant Diseases, and by Mr. Ewing on the injuries of the Brachial Plexus which can occur during operation and which have been the source of much discussion and litigation, particularly since there have been certain innovations in anaesthetic practice.

Once again we wish to express our sincere gratitude to all of our colleagues and friends who have given so generously of their time and labour for the benefit of our readers To those who sent in their contributions punctually we would offer not only our thanks but also our apologies for the many and grievous delays which have postponed the appearance of their work till so late in the year.

E. ROCK CARLING
J. PATERSON ROSS

ARTERIAL GRAFTING

By C. G ROB, *M.C.*, M.Ch., F.R.C.S.
Professor of Surgery, St. Mary's Hospital Medical School, London

AND

H. H. G. EASTCOTT, M.S, F.R.C.S.
Assistant Director, The Surgical Unit, St. Mary's Hospital Medical School, London

INTRODUCTION

Ligation of a main artery is normally followed by a developing collateral circulation whose efficiency in some cases approaches the original state. This is one of the reasons why until recent years surgical reconstruction of arteries has been so seldom attempted. A careful follow-up of patents with major arterial ligations (femoral, popliteal and so on) reveals that many of those who do not develop gangrene suffer from intermittent claudication, muscle wasting, or other symptoms of ischaemia; if the vessel is diseased ligation is still more often followed by ischaemia of the part supplied. The blood delivered by sclerotic or otherwise diseased vessels must be conserved; arterial grafting in these patients is proving to be a useful method of treatment.

Fundamental researches by Carrel (1908) into the surgical repair and replacement of arteries have provided the basis for modern practice. Fine silk suturing and refrigeration of grafts are proving as successful in man as in Carrel's animal experiments of almost half a century ago.

THE FATE OF BLOOD-VESSEL TRANSPLANTS

In most cases these function in a passive and mechanical way. An inert tube is provided which is kept open by the force of the blood flow. Within 7 to 10 days a new intimal lining is laid down by the recipient, partly from the ends of the host vessel but mostly by deposition of cells from the blood stream. If this stage can be safely passed the risk of thrombosis is usually avoided. Later failures are due to degeneration in the graft or in the artery containing it, to abnormal intravascular clotting, or to local sepsis.

Homografts—that is, tissue transplants between members of the same species—undergo a gradual process of substitution in the host. Only in exceptional circumstances can evidence be obtained of survival of the donor tissue beyond a limited period which varies according to the type of tissue and the animal in which the transplantation is taking place (Woodruff, 1952). It has been suggested (Peirce, 1952) that living arterial homografts in man may survive long enough to take part in healing; it is possible that this is so. Human homografts of skin (Mowlem, 1941) and of whole kidneys (Hume, Merrill and Miller, 1952) can survive much longer than the same tissues in experimental animals. Whether in man this survival is affected by giving ACTH or cortisone is uncertain. As far as artery grafts are concerned the [illegible] results of g[illegible] living graft [illegible] of chemically inert plastic cloth is tolerated in much the same way (Voorhees, Jaretzki and Blakemore, 1952), becoming incorporated in the new tissue laid down in and

around it by the host. The chemical factor seems to be the main reason why grafts between animals of different species (heterografts) and grafts which have been fixed or sterilized by alcohol, formalin or irradiation all give less satisfactory results in practice. Early failure or late degeneration, particularly calcification, occur much more often than if frozen homografts are used. Another important advantage of frozen homografts is that the elastic tissue survives and has been seen to function normally long after the implantation.

Autografts

Theoretically, autografts should offer the ideal method; survival is to be expected and no special storage facilities are required. In practice there are several disadvantages.

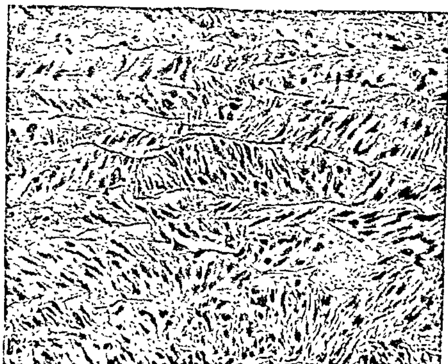


FIG 1.—Frozen carotid autograft Two centimetres of a dog's carotid were removed, frozen to $-195°$ C in liquid nitrogen, thawed and sutured back into position. Microscopy after removal 3 months later.

Artery

Carrel showed that in the dog a carotid arterial autograft, when examined months later, was indistinguishable from the normal vessel containing it. This is also true if the segment is subjected to rapid freezing and thawing before implantation (Hufnagel and Eastcott, 1952) (Fig. 1) Hurwitt and Kantrowitz (1952) have fashioned tubes from strips of splenic artery, and using these as aortic grafts in the same dog found that a normal arterial appearance is preserved months later. In man a free arterial autograft is seldom practicable. Though the spleen may be expendable, the operation of removing it with a long arterial pedicle is a major one. The increased tendency towards intravascular clotting after splenectomy might be a further hazard if a vessel of this size or smaller had been reconstructed, and one which in such circumstances could not safely be offset by the use of heparin. In the Blalock operation for cyanotic congenital heart disease successful use is made of a normal subclavian artery from the patient, but this is usually pedicled on its origin on the aorta. The splenic artery may be used in a similar way to provide a by-pass. In not all patients has the growth

of the anastomosis been sufficient. This may possibly have been because a continuous suture was used.

Vein

The first successful vein-to-artery autograft in man was reported by Lexer of Jena in 1912 for a popliteal aneurysm. This is the method most used for peripheral arterial defects. Carrel found that such grafts show hypertrophy but the thickening is mainly composed of fibrous tissue. No true arterialization has ever been known to result (Johnson and his colleagues, 1949), although this is seen in the vein distal to an acquired arterio-venous fistula. Veins contain little elastic tissue; when arterial blood pressure is admitted to a vein segment it is stretched to its fullest capacity, often even before diastolic pressure is reached; if so pulsation cannot occur. This may throw an extra strain on the anastomosis, and perhaps be a cause of early or late failure. Experimentally, Macpherson and his colleagues (1951) have found a high incidence of dilatation with mural thrombosis after inserting preserved vein homografts in the aorta of the dog Technical disadvantages of vein-artery autografting include difficulty, from lack of elasticity, in suturing the graft under the tension necessary to avoid redundancy when the blood flow is admitted (Fig. 2), and the need in some patients to sacrifice long portions of the nearby deep vein to provide a suitable graft. This is undesirable even in the normal limb, but after reconstruction of the main artery reactive hyperaemia often develops with pain and swelling which delay the return of function even when the deep veins are intact We have always avoided interference with the deep veins for this reason A large incision or perhaps even a separate one may be needed if a vein is used; this results in greater difficulty from reactionary bleeding if heparin is used post-operatively.



FIG. 2—Saphenous vein autograft for thrombosed femoral artery. Note the dilatation.

The advantages of vein grafts are that they are autogenous and not homologous, therefore they take and may live, and an artery bank is not necessary. If the saphenous or external jugular veins are used their loss causes little inconvenience to the patient. In patients with normal arteries, as in war wounds, a vein graft is preferable to an artery graft for all vessels other than the aorta and its major branches, but in patients with arteriosclerotic vessels a vein graft is technically much more difficult to suture into position than an artery graft. For these reasons we prefer artery grafts for replacing defects in the aorta and its major branches, and when the host's vessels are arteriosclerotic, whilst we recommend vein grafts for bridging gaps in peripheral vessels when they are normal in texture or nearly so

Homografts

Vein

Except that the patient's own venous system is not interrupted, vein homografts have all the disadvantages of autogenous vein grafts and none of the advantages. They were first used clinically by Blakemore, Lord and Stefko (1942) but have since fallen out of use. Where a large-diameter thin-walled shunt may be needed, as in the

around it by the host. The chemical factor seems to be '
between animals of different species (heterografts) and ;
or sterilized by alcohol, formalin or irradiation all gi\
practice. Early failure or late degeneration, particular
more often than if frozen homografts are used. Ano
frozen homografts is that the elastic tissue survives a
normally long after the implantation.

Autografts

Theoretically, autografts should offer the ideal ;
pected and no special storage facilities are require(
disadvantages.



Fig. 1 —Frozen carotid autograft Tv
removed, frozen to −195° C in lic
into position. Microscopy after remr

saline, another containing tincture of iodine, and a roll of sterile cotton-wool with which to prepare the whole of the trunk and the legs. Hairy parts should be shaved if necessary. This equipment is sufficiently compact for an unaided member of the team to take it by car to a post-mortem room away from the hospital. The whole operation of graft taking is performed with the full aseptic technique of a surgical procedure in the theatre. Several segments of thoracic aorta may be obtained, the aortic and common carotid bifurcations, and segments of assorted length of the brachial and femoral arteries. The abdominal dissection should be left until last; contamination of the instruments is then of less consequence Branches should be cut long enough to be easily ligated later, usually about one centimetre. The vessels should be cleaned down to the adventitia; adherent fat, nerves, lymph nodes and strips of vein wall should be dissected away before the grafts are stored. Meanwhile they should be put in the bottle of cold saline until ready for banking.

STORAGE

Fixation methods

Fixation methods using alcohol or formalin have been shown experimentally to give satisfactory results in rather more than 50 per cent of the cases. Where no other method of banking is at hand there might be good reason to keep some segments of this type for unexpected or emergency use. Later complications could then be dealt with if they occurred.

Refrigeration

Refrigeration at just above a temperature of 0° C. in isotonic saline is applicable to isolated and sporadic requirements where the operation can await the donor. It is sufficient to keep a bottle of sterile Ringer's solution as used for infusion in the refrigerator at all times. The graft may then be dropped into this solution and kept for several days before use. Better still is the balanced salt solution employed by Gross in his experimental and clinical artery banks at the Children's Medical Centre, Boston (Gross, Bill and Peirce, 1949) The solution used (Hanks and Wallace, 1949) is based on tissue culture requirements and contains all the plasma electrolytes, 10 per cent of homologous serum, penicillin and streptomycin. A phenol red indicator is added which remains pink unless acid metabolites reduce the pH below 7·3.

The practical results of using these fresh viable grafts in patients have been highly satisfactory Stored in this way they have provided a strong and patent channel in men and animals after several years' observation Gross has shown that they remain viable for about four weeks when stored in his bank. With longer storage after death of the artery has occurred an unknown factor of chemical deterioration comes into effect even at this temperature, and while such material may sometimes be safely used (Swan, Robertson and Johnson, 1950), there is more chance of a falling off in the quality of the results obtained as the storage time increases. This is in accord with general experience of food preservation and also with the clinical use of stored blood.

Freezing

Food kept at −17° to −20° C. or below remains wholesome for an indefinite time. If it is frozen quickly while still fresh it keeps its palatability also. The same circumstances apply to tissues for grafting, except that chemical changes in this case will adversely affect the surgical result. Since arterial grafts are scarce and the demand for them sporadic, and there is need to collect a varied selection of lengths, shapes and diameters, preservation by freezing is particularly satisfactory because of the prolonged storage which is possible. Fresh grafts kept above freezing point are a wasting asset. Peirce (1952) has kept an artery bank for a year by this method; out of 50 grafts

collected only 3 were used in patients. Our experience with the frozen artery bank at St. Mary's Hospital, London, is that the utilization rate is about 80 per cent. The only wastage is that due to errors in choosing the graft for a particular operation.

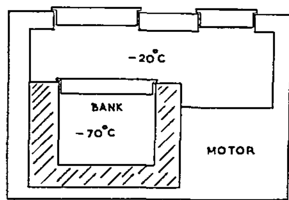


FIG. 5.—Diagram of the internal arrangement of the deep freeze.

Technique of frozen artery banking

Grafts are taken as described, and are kept in ice-cold Ringer's solution until ready for freezing. Once at this stage *several hours delay is permissible if* necessary. Meanwhile a freezing mixture is prepared in a thermos jar, using methylated spirit and adding solid carbon dioxide in small lumps, until the temperature falls to —70° C. or lower, or the freezing mixture is kept ready for immediate use in a special container in the bank. The artery bank itself (Figs. 5, 6 and 7) is kept at this temperature, therefore a small container of freezing mixture can be left in it ready to freeze grafts at any time. The human artery bank which has been in use at St. Mary's Hospital since September 1951 consists of a standard commercial deep-freeze in which is kept a cork-insulated Perspex box, divided into compartments

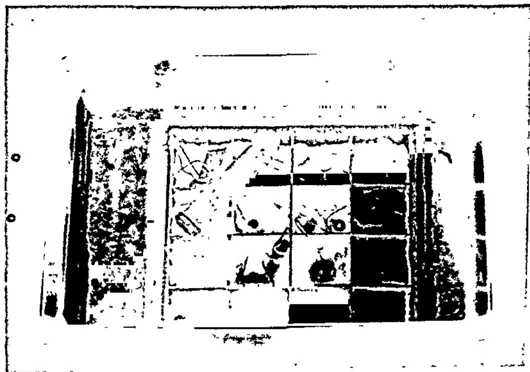


FIG. 6.—The bank open, showing the grafts in Pyrex tubes and the carbon dioxide snow.

by brass strips which contain the solid carbon dioxide and the graft tubes. The lid, a plywood box, is filled with cork chippings. This bank was made and installed by Mr. J. J. Spereall, engineer to St. Mary's Hospital Medical School. The operating temperature of the deep-freeze is about -20° C. This is probably not cold enough for very long periods of storage. It has, however, two important advantages: (1) the cold atmosphere about the bank reduces the thermal gradient to only 50° C. The

rate of consumption of CO_2 is therefore considerably lower than if the cork box stands at room temperature, a gradient of 90° C.; and (2) should CO_2 supplies fail, and this has not yet happened, the grafts could be kept frozen until the normal position had been restored. Alternatively, in the event of electrical power failure (this has been experienced) the CO_2 ice-box will maintain its low temperature for at least 48 hours.

A 25-lb. cylinder of Drikold is delivered three days a week and partly broken up for use in the bank The spare portion is kept in a lagged container for use on non-delivery days or for freezing mixtures and other laboratory purposes. Using a small sterile trolley and instruments, the grafts are cut and measured and are listed by an assistant as each is placed in its dry sterile Pyrex tube, capped ready for freezing. The tubes are then immersed in the mixture for at least five minutes and after this are transferred to an empty space in the centre of the bank. This freezing mixture

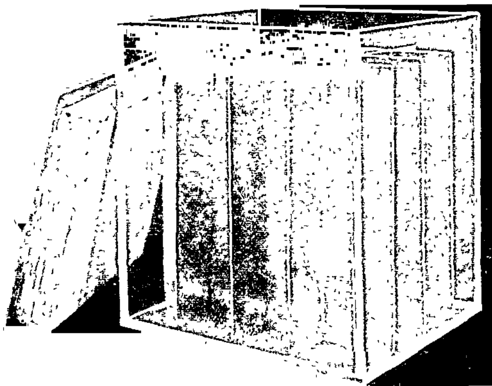


FIG 7 —Inner container, showing compartments

is not sterile, therefore only the outside of the tube should be allowed to come into contact with it. After freezing a sterile rubber cap is placed over the tube; labels are attached by which the grafts can be identified and pulled out when needed.

At the operation the size of graft required is estimated and the graft chosen is taken to the theatre in the freezing mixture since thawing must be controlled and quickly completed to avoid the formation of large ice crystals in the tissues of the graft during slow warming up to room temperature. This also conserves material because unused grafts can be returned to the bank A permanent freezing mixture container thus saves a considerable time in the preparations for either banking or using grafts. Using this method we have been able to transport grafts to other hospitals and to bring back again those which were not used. When travelling in this way it is desirable to place the freezing mixture within a large thermos jar or a special cork-lined carrying box and to be prepared for delays of several hours by having a

supply of carbon dioxide ice chippings in a smaller separate jar. A thermometer should also be taken with which to check the temperature of the mixture from time to time. Thawing the grafts is effected aseptically. The rubber cap is lifted with care, holding it and the tube with large dry abdominal packs, from the instrument trolley. Sterile *normal saline at 37° C.* (it can be conveniently kept in an incubator) is poured into the tube from a jug if the graft is frozen to its wall and the graft then floats free and is transferred as quickly as possible to a bowl of saline also at 37° C. When the graft has thawed completely it is soft and normal in appearance, both macroscopically and microscopically (Fig. 8). It is then placed in cold saline until ready to be inserted into the patient. We have found that there is an increase in diameter of about 15–20 per cent after thawing, compared with the fresh measurements. A graft slightly narrower than the artery for which it is required should therefore be chosen.

Freeze-drying

Freeze-drying is now proving to be an important advance in artery banking technique. The principle of the method is that grafts after rapid freezing are subjected

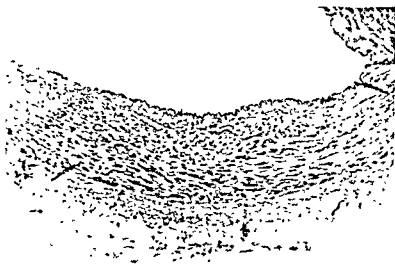


Fig. 8.—Microphotograph of human femoral artery after being kept in the bank for 3 months. The pathologist reported that it was normal in appearance.

to a vacuum of approximately 0.025 millimetres of mercury which is readily obtained by standard vacuum pump units. Water vapour can then leave the tissues freely and rapidly; this keeps the graft frozen since the latent heat of evaporation is derived from it. The vapour passes along the vacuum line and is trapped either in a glass or metal condenser kept at − 79° C. with solid carbon dioxide freezing mixture, or if only small quantities are being dried, phosphorus pentoxide can be used. As drying progresses the graft temperature rises towards that of its surroundings; when room *temperature* is reached (*in* 6–8 hours for most arteries), drying is almost completed. Most of the small amount of moisture remaining is removed by placing the graft, still in its original tube, in an evacuated desiccator for 2 or 3 days at room temperature over phosphorus pentoxide. Final evacuation is then secured by a needle passed through a specially fitted rubber stopper and the tube sealed either by coating with vacuum wax or by glass-sealing the tube itself.

While in storage the vacuum should be tested periodically, using a high-frequency spark tester. This produces a fluorescence within the tube if the vacuum has been

maintained. This test must be repeated just before a graft is used. Reconstitution of the graft should be carried out *in vacuo*, by injecting sterile isotonic saline through the rubber cap, or if the tube is glass-sealed by breaking it under water after chemical sterilization of its outer surface.

Much of the technique for freeze-drying arteries can be adapted from existing laboratory units; but it should be remembered that frozen grafts, while still fully hydrated, must not be allowed to approach melting point. It is therefore important to use either a small system which can be quickly evacuated before the graft can warm up, or to maintain external cooling of the graft tube, for example, by a carbon dioxide and alcohol freezing mixture until a drying vacuum is reached. This can be



FIG 9 FIG 10 FIG 11

FIGS. 9, 10 and 11 —Arteriograms before and after a freeze-dried artery had been inserted. In Fig. 9 the vessel distal to the block is not yet filled, a further injection with an additional two seconds delay before exposure of the x-ray film shows the extent of the block (Fig 10)

determined in several ways, the simplest is by the note of the pump. The spark tester is also used, and for research purposes a Pirani electronic vacuum gauge.

Freeze-drying of arterial grafts has been shown experimentally (Marrangoni and Cecchini, 1951; Hyatt and his colleagues, 1953) to give results which are comparable with those contained with fresh or frozen material. In man, Hufnagel (1953) and we at St Mary's Hospital have found the early results to be satisfactory (Figs 10 and 11).

The great advantage of this method of preservation is that the arteries can be stored for indefinite periods at room temperatures. This means that the surgeon can carry them in his instrument bag with as much ease as a tube of distilled water. We believe that freeze-drying will prove to be the method of choice for banking arteries.

Irradiation

Irradiation with cathode rays or by x-rays from a very high voltage source has been used in food sterilization. Bacteria are killed and the substance can be kept at room temperature. Meeker and Gross (1951) have applied this principle to arterial graft collection; highly contaminated donors can then be used, and no special precautions are needed in preparing the grafts until they are irradiated in sealed polythene containers. Oxidases and other active products of ionization within the tissues produce sufficient chemical changes to prejudice success in using the grafts. This effect can be reduced by having the tissues at −70° C during the irradiation. It is not stated whether these can then be stored at room temperature; so far storage has been continued in the frozen state. Experimentally, these grafts have been found to function well in the early stages, but calcification develops in many cases within a few months (Hui and his colleagues, 1952). It is therefore questionable whether the benefit of easy collection is not outweighed by the need for complicated physical apparatus and by the uncertain late results.



Fig. 12

Figs. 12, 13 and 14.—Angiocardiogram showing a coarctation of the aorta with a distal aneurysm in a boy aged 9 years. An aortic graft was sent from our bank in St. Mary's Hospital to St. Helier Hospital where Mr. W. P. Cleland operated, resecting the coarctation and the aneurysm, he restored continuity with the graft. The operation is shown in Figs. 13 and 14.



Fig. 13

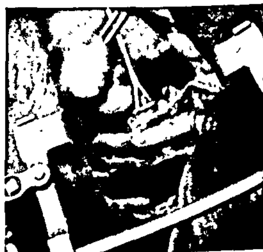


Fig. 14

INDICATIONS FOR ARTERIAL GRAFTING

Grafts are now used for the restoration of traumatic and congenital defects of large arteries, for aneurysms, malignant invasion and the localized occlusions which occur in arteriosclerosis.

Congenital malformations

When congenital malformations occur in the *heart and great vessels* they are often suitable for surgical correction. The last ten years have brought coarctation of the aorta and congenital cyanotic heart disease into the surgeon's field. While direct procedures are preferred, some types require a free arterial graft, usually where there is insufficient normal vessel or it is too immobile for a direct anastomosis. Some cases of subclavian-pulmonary artery anastomosis and many excisions of long coarctation (Gross, Bill and Peirce, 1949) have been completed with the help of an arterial homograft. Aneurysm formation beyond a coarctation generally requires excision and grafting (Figs. 12, 13 and 14) *Peripheral anomalies* of the vessels are generally in the form of multiple arteriovenous fistulae and these are usually too many and too small for a direct attack upon them to be worth while. Moreover, these fistulae are often present within the bones. Occasionally, such a patient may have a localized lesion and then a graft may be indicated. Efficient arteriography helps to settle this point.

War wounds

In World War I it was hoped that Carrel's principles for the repair of blood vessels might find application to military surgery. Under field conditions, however, the complications of infection, haemorrhage and thrombosis developed in so many patients that repair was abandoned in favour of ligation and, in most cases, amputation. In World War II, even though chemotherapy and heparin had arrived, it was found to be difficult to carry out such exacting surgery in the forward areas where it was most needed. A few limbs were saved by the use of vein grafts using the Vitallium tube non-suture technique of Lord and Blakemore and a few vessels were repaired with a direct anastomosis, but on the whole reconstructive surgery was confined to rear areas in patients with aneurysms. Stammers (1945) summarized the gloomy position of primary ligation under battle conditions when he reported that of 31 femoral ligations 68 per cent required amputation, and of 36 popliteal ligations 72 per cent. In Korea these difficulties were overcome and an efficient method of vascular reconstruction was introduced in the forward areas Field surgeons were given a short course of practical instruction in vascular anastomosis and vein grafting on dogs. As a result, by the late summer of 1952 more than 40 injuries of major arteries (femorals, popliteals and so on) had been repaired by saphenous vein autografts and 35 of these grafts remained patent These patients did not receive heparin—a great achievement!

Traumatic aneurysms and arteriovenous fistulae in battle casualties

Penetrating wounds of the major blood-vessels are the main cause of death in battle. In most of these wounds rupture of a large vessel in the thorax or abdomen is sustained. Patients with major arterial wounds who survive long enough to be brought in are likely to have an injury to one of the peripheral vessel bundles, and about 50 per cent of these involve the iliac, femoral or popliteal arteries. The accompanying vein is so much thinner that arteriovenous injury with establishment of an arteriovenous fistula is rather commoner than false aneurysm from damage to the artery alone. For an aneurysm or fistula to form the wound must be small and usually must have escaped excision, healing follows and days, weeks, months or even years later the aneurysm or arteriovenous fistula is noticed.

Management of traumatic arteriovenous fistula and false aneurysm

Most authorities have agreed that a "waiting period" of three months should be observed, because in the meantime a collateral circulation is set up and the local tissues soften as the traumatic reaction subsides (Maybury, 1944). There is perhaps less risk of renewing a dormant infection than in the early stages. The most serious threat is that of an enlarging false sac which progressively affects the surrounding collateral vessels, the distal part of the limb suffering in consequence. Either a false arterial sac or a varicose aneurysm may do this, but the latter grows more slowly because of the decompressing effect of its fistula. Operation, therefore, can often be further delayed in arteriovenous fistula. In very small aneurysmal varices there may be no indication for operation if the condition is non-progressive and symptomless.

Ligation operations.—These have been the standard practice, preferably when the collaterals have been allowed time to develop. Preliminary sympathectomy is often performed just before the main intervention, but this may have the effect of shunting blood away from where it is needed—in the main collaterals (Cohen, 1952) When possible quadruple ligation has been performed. Proximal arterial ligation alone for a peripheral fistula must never be performed; the risk of gangrene is too great from draining of the limb through the enlarged vessels leading back through the fistula.

Reconstructive surgery.—Reconstructive surgery in traumatic aneurysm and arteriovenous fistula was limited in World Wars I and II, with only a few exceptions, to repair of the arterial defect through the vein or false sac as used by Makins. Mason Brown (1946) repaired the artery on 19 occasions at his vascular injuries centre in Italy; none of these patients lost their peripheral pulses after the operation. Over the same period he performed a ligation operation on 30 occasions and in 9 patients the aneurysm was excised.

The campaign in Korea has provided an opportunity for new reconstructive methods to be tried. Seeley and his colleagues (1952) have reported their experience of 101 patients with aneurysms following battle injuries from this theatre. A reconstruction was accomplished in over 50 per cent of the major vessels operated upon, either by arterial repair and anastomosis, vein grafting or artery grafting. No anticoagulants were used. Of the 90 patients operated upon, 64 had a major vessel lesion. Just under 25 per cent of the patients who had ligation operations developed arterial insufficiency compared with 2·8 per cent of those in which reconstruction was performed. In nearly 50 per cent of the lower limb cases after ligation the arterial supply was insufficient. It is noteworthy that in two cases of reconstruction of the common femoral artery with sacrifice of the vein, symptoms of chronic venous insufficiency developed. This aspect of arterial restoration will again be referred to in the section on arteriosclerosis.

Non-traumatic aneurysms

Most fusiform aneurysms of the aorta and major peripheral arteries develop so slowly that the arteriosclerosis which is their cause represents a greater danger to the patient in the other situations affected, such as the heart or brain. Though these dilatations may be technically operable it is seldom necessary to remove them. If they cause pain or are thought to be growing, some buttressing procedure such as the insertion of steel wire (Linton, 1951) or the perivascular injection of dicetyl phosphate in olive oil (Berman and Hull, 1952) may be tried with little risk of inducing thrombosis and a fair prospect of limiting further expansion.

Saccular aneurysms rarely arise from a pathological defect in the side of a large vessel, but when they do they may well be cured by resection and local repair. More often the whole artery is affected and will need to be resected with reconstruction by an arterial homograft. In situations such as the arch of the aorta where large branches arise from the sac it is not at present possible to reconstruct the affected

section even with a duplicate homograft. This has been attempted experimentally (Hardin, Batchelder and Schafer, 1952) but with a formidable mortality even though temporary plastic tube shunts were used to maintain the distal circulation during the procedure. For such aneurysms the best treatment is probably still to insert steel wire or one or more Colt's umbrellas.

For such anatomical reasons the only pieces of aorta which can at present be resected are those lying between the left subclavian artery and the diaphragm (Brock, 1952) and below the renal artery down to and, if necessary, including the bifurcation (Dubost, Allery and Oeconomos, 1951).

Saccular aneurysms of the iliac and other large peripheral vessels, whether traumatic or not, are often densely adherent to important surrounding structures. If they can be safely excised an arterial homograft may be inserted into the resulting defect. If not the operation is conducted as though an endo-aneurysmorrhaphy were intended, except that an inlay graft is inserted into the narrowed channel produced (Gerbode and his associates, 1952).

Popliteal aneurysm. this is the commonest peripheral site. If saccular these steadily enlarge and cause vein and nerve compression, later the collaterals are also obstructed. Rupture is a disastrous complication This lesion should therefore be treated radically. Lexer (1912) was the first to replace the aneurysmal popliteal artery by a saphenous vein graft, Murray (1939) also performed this operation using heparin post-operatively for the first time Martin and Lynn (1952) in Great Britain have removed a syphilitic popliteal aneurysm and restored the defect with an infant's aorta.

Mycotic aneurysms are associated with a septicaemia, usually bacterial endocarditis. Before the introduction of antibiotics they were nearly always fatal. Today some of these patients survive and the aneurysm becomes a surgical problem. Brock (1952) has resected a mycotic aneurysm of the thoracic aorta associated with a coarctation and successfully bridged the defect with an arterial graft.

Neoplasms

Primary sarcoma —Primary sarcoma in the limb, particularly fibrosarcoma of the soft tissues of the thigh, may involve the main artery in the region; though this attachment can often be divided by sharp dissection local recurrence is likely and amputation then becomes necessary. This, and a limited number of other primary cancers near large vessels, particularly if they are only locally malignant, are perhaps suitable for excision of the artery and homografting the defect.

Carotid body tumour.—The decision to sacrifice the densely adherent bifurcation of the common carotid is a serious one; a simple tumour may be rendered inoperable, a malignant one would be incompletely removed. Arterial grafting would be ideal for this situation. A bifurcation can be inserted, but all that is necessary is an end-to-end common to internal carotid reconstruction with an arterial homograft to close the gap.

Secondary carcinoma.—In block dissection of the glands of the neck at a late stage in the procedure operability may be found literally to hinge upon the carotid artery to which the last few glands are closely adherent. In these elderly patients a carotid ligation is almost certain to bring about a hemiplegia

Resection of the involved segment of carotid with restoration of the gap with a suitable graft can be used in this instance; occasionally, in a very tortuous carotid, simple end-to-end anastomosis is possible, it being remembered that a certain amount of tension is desirable in arterial anastomoses In this situation, as in the normal thoracic aorta, occlusion should be allowed only for as short a time as possible. The graft should be inserted over an indwelling plastic tube so that its function may continue for the greater part of the time taken in suturing the two ends. The second half of the second anastomosis is made using untied slinging mattress sutures, the vessel

above and below the tube is clamped, the tube removed and the re
tied. The clamps are then released and any additional haemostatic sut
be needed are then inserted.

Civilian injuries

In civilian surgery injuries causing division of the main artery
except as the result of plate glass and factory machinery accidents. It
for an inexperienced surgeon to divide the common femoral artery in
saphenous vein ligation operation. Repair by anastomosis has bee
several such cases, but if a length of artery has been damaged by a
graft may be necessary.

Chronic mechanical factors are more often responsible for blocka
peripheral arteries. For example, the vascular symptoms of cervical
by Eden (1939) to be due to local compression of the axillary artery as
first rib behind the clavicle At this point an aponeurotic band form
one of the scalenus muscles often exerts localized pressure upon the a
lead to thrombosis or to aneurysm formation. A murmur is often audit
(Edwards and Levine, 1952). Relief of the cause is usually sufficient
true aneurysm may require excision and grafting if producing sym
ample, emboli to the hands (Lewis and Pickering, 1934).

Primary arterial thrombosis

This condition (Learmonth, Blackwood and Richards, 1944) oc
adults who show no evidence of arteriosclerosis. It is thought that in
there may be some disturbance in the mechanism which normally
vascular clotting, either in the blood itself or in the arterial lining. Th
also occurred after intravenous injections and infusions without an
locally. There is probably a mechanical factor in the production of th
example, the hard aponeurotic margin of the inguinal ligament may ca
iliac thrombosis, behind the joint line of the knee the artery is simila
this type of wearing stress (Figs. 15 and 16). It is important to reme
as after a formal ligation operation, so after these spontaneous localiz
the effect on the extremity produced by interruption at the popliteal
greater than that which develops after external iliac blockage (Halsted,
1919). Closed injury to the popliteal artery is a serious lesion which co
cases of dislocated knee joint (Reid and McKenzie, 1952). Gangre
ischaemic symptoms such as intermittent claudication are likely to foll
a more active attitude to these injuries is to be encouraged.

Traumatic arteria spasm

Kinmonth (1952) has shown that this previously refractory condi
better to the local application of a 20 per cent papaverine solution tha
local or intravascular drug. When it occurs as a complication of
fracture it may become impossible to alleviate; Volkmann's ischaem
then results (Griffiths, 1940). Papaverine locally may prove to be the
difficult problem. Certainly excision of the segment alone should no l
tised. Grafting of the gap should always be performed if drugs fail a
required.

Arteriosclerosis

Morbid anatomy and physiology

In the past, study of amputated specimens showed little more than
stem artery was extensively blocked by a long organized thrombus and g

thickening. Calcification may be extreme yet the artery remains patent. Earlier stages and the body's reaction to them were not appreciated until it became possible to examine the arteries *in vivo* by angiography. Boyd and his colleagues (1949) have stressed that localized occlusion of the main artery is the usual early lesion of the arteriosclerotic leg; it is present in most patients with intermittent claudication. These localized blocks occur in fairly constant sites: the lower abdominal aorta and iliac arteries (Kekwick, McDonald and Semple, 1952), the ilio-femoral junction, the superficial femoral artery in Hunter's canal and at the foramen in the adductor magnus where the artery is thought to be subjected to localized wear and tear which condenses the arteriosclerosis in this segment. From here it may spread up or down, popliteal involvement produces more disability than femoral. Most of the thigh muscle blood supply arises from the profunda femoris; in a femoral block these muscles therefore continue to work normally and a good collateral circulation is



FIG 15

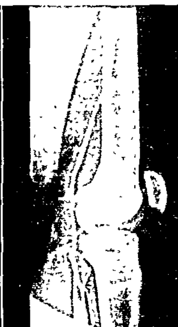


FIG 16.

provided which re-enters the popliteal trunk and prevents serious reduction in distal blood supply. If the popliteal artery is blocked a bottleneck is produced for which there is no adequate alternative route. A cold foot and quite severe claudication are usual in these cases, even in younger patients. It seems to occur fairly frequently in patients under the age of fifty years. The mechanical factors responsible are probably the same as those which were described by Learmonth, Blackwood and Richards (1944) and Boyd and his colleagues (1949) in "primary popliteal thrombosis" of young patients, and are mainly the effects of strain at the level of the knee joint.

The limit of these early lesions is determined by the anatomy of nearby principal branches. Much depends upon the state of these, for they should be able to take a large part of the necessary collateral blood flow. If they are diseased an attempt to perform their function is made by many of their own branches and by similar branches of the main vessel arising farther from the block. These long tenuous collaterals

clearly cannot provide the same pressure of blood below the block as a small number of short direct channels (Cohen, 1952). A return of distal pulses may even occur in the latter type though they are likely to disappear after exercise which causes the limited blood supply to be almost wholly shunted into the muscles.

Natural phases of improvement are the rule after each of the acute episodes by which the disease tends to progress. They are due to the development of collateral channels; only the spread of the disease across the mouths of these or into their course can check this spontaneous improvement. If patients with intermittent claudication are kept under regular observation their exercise tolerance will be found to vary in this way. Hamilton and Wilson (1952) have pointed out that therapeutic trials in this disease have generally not taken these factors into account. In carefully controlled observations they could find no significant effect to have been produced by any of the accepted methods of medical treatment, other than rest in bed, the treatment of anaemia and perhaps stopping smoking.

Effects of sympathectomy

This results in a general release of vasoconstrictor tone in the smaller vessels of the part which has been denervated. It has been shown by Lynn and Barcroft (1950) that after sympathectomy the increase in limb blood flow is greatest during the first 48 hours, but that after a week a more normal level is resumed.

As a means of improving the muscle blood supply, however, there is little to be said for sympathectomy. In our opinion claudication is not relieved by it because the volume of blood needed by exercising muscle is of the order of 20–40 cubic centimetres per 100 cubic centimetres of calf per minute as compared with 2–7 cubic centimetres at rest (Shepherd, 1950). This latter figure diminishes with age and declining general activity.

The structural lesion in the main vessel acts as a bottleneck, preventing these large quantities of blood from reaching the active muscle when it is needed. The only means of reversing this state of affairs is to wait in the hope of an adequate collateral circulation developing itself or, more rarely still, recanalization, or to substitute a vein or arterial graft for the blocked segment; this is the most certain way of restoring a blood flow which can provide for all the needs of normal activity.

TREATMENT OF ARTERIOSCLEROSIS

Direct surgical treatment

The majority of patients on first developing symptoms of ischaemia of the leg can be shown to have a localized block in the main artery which would be anatomically suitable for artery grafting, but it must be remembered that arteriosclerosis is a generalized disease; many patients whose only symptoms are in the legs also have coronary or cerebral arterial disease. There is no purpose in relieving intermittent claudication if angina pectoris substitutes a similar or worse limit to the patient's activities. Mental deterioration due to cerebral vascular degeneration may also restrict the working capacity so seriously that claudication is no longer a serious symptom. Kekwick (1951) found that of 45 patients with claudication 9 had angina pectoris, 5 had a past history of cardiac infarction and 3 had suffered cerebrovascular accidents. It is only when the local manifestations of leg arteriosclerosis dominate the picture that direct surgical intervention should be considered. If it can be established that local mechanical factors are mainly responsible, that there is no clinical sign of arterial insufficiency elsewhere and the patient's symptoms are sufficiently severe, then a reconstruction operation is indicated.

These special requirements apply only to the treatment of intermittent claudication. When gangrene threatens or has actually developed a lower standard of general

fitness can be admitted. Usually the only alternative to an attempt at reconstruction is amputation. As generally performed, the site of section is through the blocked portion of the femoral artery. This operative finding tends to justify the procedure in the surgeon's mind, although there might have been a patent main artery below this point. In such limbs it is the collateral circulation which provides distal nutrition. When these vessels fail through disease the only chance of saving the limb is to restore the main artery (Fig. 17). On four occasions we have restored the main artery in patients with gangrene by a blood-vessel graft. One with a gangrenous great toe is well one year later; a second and third, recorded at the end of this paper, and the fourth who had a saphenous vein graft thrombosed this on the seventeenth post-operative day.

Diabetes is an important factor in the progress of leg ischaemia. Arteriosclerosis is commoner among diabetics than in others of the same age. Infection plays an important part; it tracks along the deep structures of the sole of the foot where it is hidden and may fail to be recognized. As a result the damage to the limb is greater than if the patient was non-diabetic, and the insulin requirements rise steeply When infected tissue planes have been opened up and sloughs removed the diabetes is more easily controlled. As with most operations, diabetes increases the risks. These must be set against the probable benefits of restoring the circulation and the otherwise inevitable danger of the alternative, an amputation.

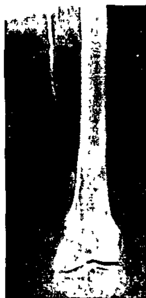


FIG 17—Arteriogram from a patient, aged 25 years, with gangrene of the foot

Careful examination of the pulses in the main vessels of the limb will indicate whether reconstructive surgery is possible; if the pulse at the ankle can be felt, conservative treatment may suffice, and it must be pointed out that this clinical picture is not infrequent in diabetics. If, however, the pulse is lost in the more proximal arteries, grafting may be indicated.

In assessing any patient for direct surgery the decision must be made against a background of the general situation. Some idea should be formed, if possible, of the natural tendency of the arteriosclerosis in that particular individual. In most instances time alone brings a return of collateral blood flow. The effectiveness of this is the best guide to treatment It is worth while to adopt some simple standard exercise tolerance test with which to measure the patient's capacity for muscular work on successive visits. A particular flight of steps or a constant circuit are suitable. The amount of exercise and the rate of its performance are recorded. Fluctuations occur in the natural course of the disease. Rest in bed is one of the few positive methods of improving exercise tolerance by non-operative means.

Arteriography

In treating disease of the large and medium sized arteries direct surgical reconstruction by grafting cannot usually be undertaken without detailed radiographic information on the distribution of the disease, which may be obtained by percutaneous injection with diodone of the main peripheral trunks, or of the abdominal aorta itself. Complications are few, an inadvertent periarterial injection is usually harmless and removal of the diodone from the soft tissues is quickly completed.

Diodone (Diodrast, Perabrodil, 3 : 5-Diiodo-4-pyridone-N-acetic acid and diethanolamine) is supplied in 35, 50 and 70 per cent strengths. All are suitable for peripheral arteriography in doses of up to 20 millilitres. Aortography is best

performed with the 70 per cent solution using 30 millilitres or more if the injection can be made sufficiently quickly. No special equipment is needed. Portable x-ray machines are sufficient for the limbs; a rather long exposure is used. For the trunk a rapid exposure is needed, one large picture is taken in the x-ray department itself.

Technique of femoral arteriography

General anaesthesia is preferable if the higher concentrations of diodone are to be used. One painful stimulus of the contrast medium within the vessels is sufficient to cause movement unless sufficient depth or relaxation has been obtained. The two cassettes or a single long one are placed beneath the limb which is slightly externally rotated. A doubly intensifying screen is used over both films; the thigh film should have the faster emulsion. The machines are centred accurately by measurement, this depending upon a previously known estimation of the "spread" of the two machines. The contrast solution is drawn up into an ordinary 20-millilitre syringe which is fitted with an 18-gauge hypodermic needle 2–3 inches long. With an assistant ready to compress the external iliac vessel, the common femoral artery is entered where its pulsation is most clearly felt, usually just below the inguinal ligament. Compression is now applied above this and the full injection made. The first picture is taken on completion of the injection. As the exposure finishes the radiographer says "release" and the compression is removed. A three-second exposure of the calf and foot follows almost at once using the lower machine. This method gives good results in all cases except those with severe arterial deficiency, in whom it is best to make the injection into the pulsating femoral artery, the pictures can be taken with two machines as described above, or a single tube may be used to cover the entire limb. In the lower limb the normal arterial tree is direct and continuous with smooth curves and most branches are shown at rather acute angles to the main stream. Few vessels fill in the thigh apart from the femoral and the profunda femoris which is narrow in the resting state. If the profunda is dilated an obstruction to the main trunk is usually responsible. This appearance is reversed by successful arterial reconstruction (Figs. 18 and 19). Anatomical abnormalities are rather uncommon, the two most often seen being a high bifurcation of the popliteal artery, and absence of the dorsalis pedis. These findings may correct errors in clinical [illegible]ion.



Fig. 18 Fig. 19

Figs 18 and 19.—Arteriograms of a successful reconstruction with the patient's saphenous vein. Note the disappearance of the collateral circulation through the profunda femoris.

Aortography

The abdominal aorta is best demonstrated by percutaneous injection. Seven-inch 15-gauge or 17-gauge needles soldered to a three-way tap and connected to a 25-millilitre syringe are used (Fig. 20). The needle is introduced from the left renal angle and advanced in an inward and slightly upward direction (Fig. 21) The lumbar body is located as in paravertebral sympathetic injection and the needle advanced tangentially beyond it; the aorta is easily located both by the slight jerk as it is entered and by a spurt of arterial blood when the three-way tap is turned so that the end hole is open. The whole set is filled with 70 per cent diodone before the needle is inserted. The injection should be made as quickly as possible (for example, 10 millilitres per second) and on completion the radiograph is taken. Good pictures are obtained even in obese

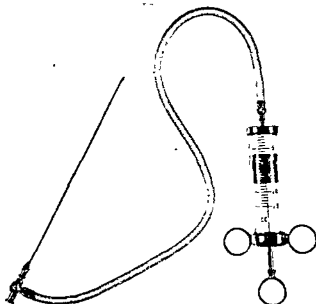


FIG. 20 —Syringe, plastic tube and 17-gauge needle used for aortography.

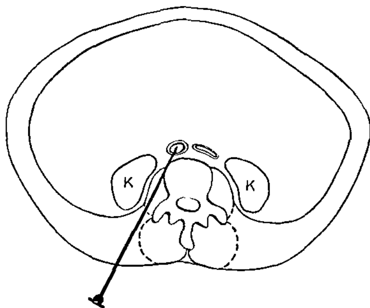


FIG 21 —Diagram of the path of the needle in a lumbar aortogram.

patients (Fig. 22). Images are also obtained of the vessels of the abdominal viscera, notably the renal and mesenteric arteries. A higher injection can be made if abdominal vessels are particularly required. This is a safe, easy and reliable method.

Thoracic aorta. Angiocardiography offers a satisfactory method of outlining the arch and upper descending aorta.

Reconstructive operations for arteriosclerosis

The three alternatives are (1) to remove the obstruction from the affected segment *in situ*; (2) to excise this piece completely substituting a vessel graft; or (3) to provide a by-pass.

Thrombo-endarterectomy or disobliteration

In 1947 dos Santos described a method for enucleating the diseased core from such arteries by finding a plane of cleavage in the media, the atheroma and its organized



Fig 22



Fig 23

Figs. 22 and 23 —Pre-operative and post-operative aortograms showing a successful thrombo-endarterectomy of the common iliac artery.

thrombus was removed together with the adherent intima and some of the inner elastic fibres. He used a special probe inserted through a series of transverse incisions in the artery.

Leriche and Kunlin (1947), Bazy and his associates (1947, 1949), Huguier (1948), Fontaine and Hubinot (1950) and several other French and Belgian surgeons have recorded a large number of these "disobliterative" operations performed mainly for claudication. In most patients a single longitudinal incision in the artery was used. After dissecting out the obstructing material the vessel was repaired by a continuous arterial suture along the whole length of the arteriotomy.

We find that this can be a difficult closure, and an insecure one. Haemorrhage from it is likely to follow, particularly if the incision is long. The vessel is often narrowed by this repair, and since the lining of the channel is formed by ragged elastic tissue thrombosis is also common. Heparin is necessary to prevent this but brings its own complications.

A fairly high early failure rate and an almost prohibitive incidence of loss of limb and sometimes life have generally followed the use of this method. Fontaine and his

grafting an artery should be used. Much of its elastic tissue will survive the homotransplantation; dilatation and rupture, perhaps for this reason, do not occur. These complications have been reported after vein grafting the abdominal aorta.

Types of vein graft.—Kunlin (1949), in order to avoid sacrificing the collateral arteries which join the main vessel at the upper and lower faces of the obstruction, used a *parallel shunt*, with end-to-side anastomosis performed away from these important branches. Martin (1952) has also used this technique but is not satisfied with the late results. It is against the principles of vascular surgery to create turbulence in the blood flow. This is why end-to-side junctions so often thrombose.

Sacrifice of the deep vein.—This has often been performed to provide a suitable graft from the same incision. We feel that this is not justifiable. After successful reconstruction of the artery a marked hyperaemia develops in the formerly ischaemic tissues and abnormal demands are made upon the venous return. If this is impaired because of vein resection symptoms of venous insufficiency will trouble the patient at this early stage, and may later persist, causing chronic painful swelling of the calf and ankle. Transvenous closure of an arteriovenous fistula and artery grafting for false aneurysm using the nearby vein are known to produce this type of disability. It is perhaps a more difficult one to treat than the arterial condition which indirectly led to it.

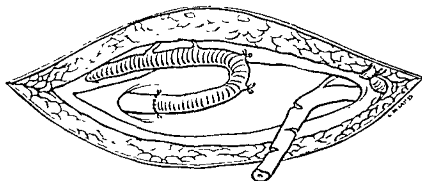


FIG. 24.—Technique of ensuring that a saphenous vein graft has the valves facing downwards (after Julian and his colleagues)

Saphenous vein grafts.—The size of the internal saphenous vein is rather variable, *but in the older male patient with whom we are principally concerned there is usually* no difficulty in matching the vein to the femoral or popliteal artery. It may contract during manipulation, or the surgeon may, in error, suture it into the artery with its valves facing upwards, and it is apt to dry out during the focusing of interest upon the performance of one or other anastomosis. Julian and his colleagues (1952) have devised a neat method of avoiding these difficulties. The internal saphenous vein is exposed in the same wound as the thrombosed artery. It is divided between ligatures at the lower end of the incision and this end is sutured to the cut end of the artery which has been divided above the block. This temporary arteriovenous shunt is then allowed to function for a few minutes (Fig. 24), the graft is accommodated to the arterial blood pressure, and since its valves must face downwards, free passage of the blood flow can occur. The operation is completed by detaching the saphenous vein above and swinging it down to be anastomosed to the lower stump of the recipient artery.

These authors have used the technique described in 18 patients. In one of these both superficial femoral arteries were replaced successfully. In 6 the operation failed, 2 amputations were required and one patient died of a post-operative coronary thrombosis whose graft was found to be patent at autopsy. Twelve patients had a return of foot pulses with complete relief of intermittent claudication. For iliac occlusions they employed thrombo-arterectomy, and in several cases with femoral

thrombosis the femoral artery was partly disobliterated above and below the obstruction in order to preserve collateral vessels. Transverse incisions were used as originally recommended by dos Santos.

Our experience of using vein grafts in this disease is small, but we have found them difficult to insert, lacking the elasticity of an artery so that close matching of the diameters and insertion under tension were not possible. They generally dilate under the arterial blood pressure (Fig 19). They are, however, available at any time without the need for banking facilities, and being autogenous they should, in theory, survive, though they do not "arterialize" as Carrel thought. It has recently been suggested (Hufnagel, 1953) that live grafts whether autogenous or homologous are more likely to clot than dead grafts. Experimentally it has been shown that clotting is more likely to occur in the host's own artery when damaged, or a live graft than in a dead graft. The reason may be that the intima of a dead graft has no electrical potential whilst a live graft or a damaged artery has a positive potential.

Arterial homografting

In most of our reconstructions of the lower limb arteries we have made use of homografts of frozen artery. Arterial homografts had not, as far as we know, previously been used in the limbs in man, perhaps because they are difficult to obtain unless a method for their long-term storage is used. The ease with which they can be inserted and the anatomical result as judged by post-operative arteriography compare favourably in our experience with vein grafting. It is worth trying to use a vein whenever possible; but most arteriosclerotic recipient vessels will need an arterial graft. Meanwhile the frozen arteries in the bank can be kept for as long as necessary.

Preparation for operation

The selection of patients for reconstruction has already been discussed. It should be stressed again that in patients with intermittent claudication the decision to operate is made with the patient's requirements and his general condition constantly in mind. In gangrene, however, in most cases all that is necessary is an anatomically suitable block.

Important preliminaries to operation include: (1) general medical assessment; (2) exercise tolerance tests; (3) tests of circulatory function; (4) arteriography; (5) blood grouping; and (6) review of the contents of the artery bank. We include all these in each patient considered for surgery.

General medical assessment

It is important not to operate upon patients with regard only to their arteriographic findings. A careful survey should be made of the rest of the cardiovascular system; for example, a small block in the apparently normal opposite femoral artery, or in a coronary artery, will probably give rise to symptoms when the load of exercise has been transferred to them should restoration of the presenting lesion succeed. Thorough history taking and accurate observation of the peripheral pulses will usually exclude these complications. In case of doubt a physician's opinion is essential, particularly in diabetes. An electrocardiogram is usually advisable.

Exercise tolerance tests

It is often difficult to judge the natural course of senile ischaemia of the lower limb. The patient's view of various treatments is coloured by factors other than their effectiveness, particularly when this is doubtful. Exercise tolerance is easily measured by getting the patient to walk or climb some set distance on successive occasions. Within a natural variation, the cause of which cannot be explained, the general

tendency of the disease can usually be assessed. Surprising results are often obtained; collateral circulation may fail to develop in a young patient, but in an older one time may bring a return of distal pulsation. This may be due to recanalization or to the development of an exceptionally efficient collateral circulation.

After successful reconstruction of the main artery there is no doubt about the restoration of function; the exercise tolerance test can be performed without limitation of any kind. It is useful in a patient whose graft has failed to estimate the final effect of the operation. Usually there is little difference in the patient's idea of his exercise capacity, though an unexplained improvement is fairly common in most published cases. In few of these has it been measured in terms of a standard exercise tolerance test.

Tests of circulatory function

Cutaneous reactive hyperaemia.—This test (Pickering, 1933) gives a clear and measurable indication of the efficiency of the distal circulation. The rate at which a reactive skin flush spreads down the normal leg after temporary arterial arrest is directly proportional to the force behind the small vessels. The table below shows the results of the reactive hyperaemia test before and after a successful artery graft.

TABLE

RESULTS OF REACTIVE HYPERAEMIA SKIN TESTS IN A PATIENT WITH INTERMITTENT CLAUDICATION BEFORE AND AFTER RESTORATION OF THE OCCLUDED POPLITEAL ARTERY BY AN ARTERIAL GRAFT

	Patellar tubercle	*Malleoli*	*Toes*
Before operation	8 secs.	28 secs.	47 secs.
After operation .	2 secs.	6 secs	8 secs.

Oscillometry.—A doubtful pulsation in an ischaemic leg is of no diagnostic value, since that of the vessels of the pulp of the examiner's fingers generally obscures the patient's. In such circumstances the oscillometer gives visual information which can also be recorded as a graph. Comparison with the normal limb is necessary. The recording cuff can be placed in turn above and below the knee; this record may help to localize the obstruction in the main artery. Diminished pulses usually disappear altogether after exercising the affected limb. This was clearly demonstrated by tonoscillometry (Kekwick, McDonald and Semple, 1952). In the early hours after a grafting operation the pulses may be difficult to feel in either lower limb although the blood may be normal. Oscillometry is useful in determining the function of the graft at this time

Plethysmography.—Though perhaps mainly of research interest, this investigation gives direct and graphic evidence of the volume of blood flow in the limb which greatly enhances the surgeon's understanding of what is happening in the extremity. A regular pattern of responses is seen in health, and in mild and advanced arterial deficiency this is found to be considerably altered. These phenomena will be summarized

(1) *Cutaneous blood flow in the foot.* The foot is placed in a plethysmograph filled with water at 45° C., as described above in the reactive hyperaemia skin test; the object of this is to induce maximal vasodilatation. Immersing the hands likewise reinforces this effect. The blood flow is then recorded at intervals for a period of up to 30 minutes. In health the curve obtained in this way rises steadily for 20-25 minutes reaching maximum values of 20-25 cubic centimetres of blood per 100 cubic

centimetres of foot per minute. In the ischaemic limb, soon after a femoral or popliteal arterial thrombosis, the early recordings show low rates of flow and do not increase while the foot is immersed in hot water. In such cases this test may cause pain or cyanosis to develop.

After a successful operation the blood flow to a previously ischaemic foot is many times normal (Fig. 25). This hyperaemia may produce pain and need exposure and

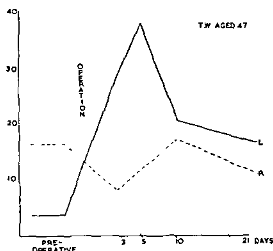


Fig. 25.—Blood-flow study showing hyperaemia after a successful graft.

cooling applications for its relief, in the same way as is needed by a recovering trench or immersion foot.

(2) *Calf blood flow.* With the calf placed in a plethysmograph and the foot circulation arrested by an arterial pressure cuff at the ankle the resting blood flow is measured with the water at 34° C. Cutaneous hyperaemia is therefore avoided and it is mostly the muscle blood flow which is measured. It is difficult to do this with

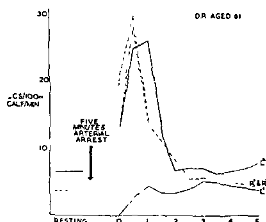


Fig 26 —Reactive hyperaemia through calf muscle before and after a successful artery [illegible]

the muscles at work, though Shepherd (1950) has succeeded in doing so, finding that the muscle blood flow during brief strenuous exercise immediately increases, then falls almost as rapidly to resting levels. Much the same pattern of hyperaemia and resolution is found to occur after five minutes of arterial arrest above the knee (Lewis and Grant, 1925). Fig 26 shows a typical chart of this response in both legs of a patient with a blocked left superficial femoral and popliteal artery. Following an arterial graft operation the left calf flow now shows the normal type of response to temporary arterial arrest. Intermediate types of curve may indicate a narrowed but

not completely obstructed main arterial channel, such as a recanalized thrombus or an unusually efficient collateral circulation.

Arteriographic findings

This investigation forms an essential part of the pre-operative assessment. A method for femoral arteriography has already been outlined. Study of the diodone shadows of unaffected portions of the femoral or popliteal artery gives some idea of the severity of the arteriosclerotic process. The distribution of collaterals can be seen in detail and later, at operation, this information is most helpful.

Occasionally, more particularly after attempted disobliteration, the main vessel appears on arteriography to have been restored, but pulses below this level do not return. If the profunda is seen still to be dilated, the operation is unlikely to have been a complete success.

The condition of the main vessel below the block is, in our experience, a critical factor. Arteriography proves little more than the presence of a patent channel and a possible site for the lower anastomosis of a graft. It often fails even to do this, particularly in patients with gangrene of the extremity where an insufficient collateral stream cannot carry the diodone into the open vessel below. A ghost-like appearance of this portion of the artery can be due either to a trickle of the contrast medium into it through a small collateral, or to a serious narrowing in the lumen from atheroma or a thrombus. An impression can be formed of the state of the arterial wall in the lower portion, and of the chance of performing a successful anastomosis with it, but in most cases this assessment must be made on the basis of the operative findings. It is usually the most difficult and uncertain part of the operation. In many patients failure to demonstrate the artery distal to a block means that the arteriogram has been taken too soon after injection, in such a case a second injection with a longer interval before the film is exposed may show the extent of the main vessel block (Figs. 9 and 10).

It is important to know the extent of the disease in the calf and foot vessels; arteriography in patients with intermittent claudication will usually show these, but in those with gangrene it seldom does; an injection into the patent lower channel at the time of operation is substituted for collateral filling. Operation, either a graft or an amputation, is usually necessary in these patients so that little is lost.

Blood grouping

It is necessary to have a reserve of compatible blood ready. In these patients a steady ooze from the soft tissues begins soon after the first heparin injection given during the operation, and often continues until the heparin has been discontinued. This occurs in spite of the most careful control and with regional as well as systemic heparinization. Dextran and other substitutes can also be used in order to prevent a fall in blood pressure which would favour thrombosis of the graft.

Review of the artery bank

The arteriograms are inspected and the length of the blocked arterial segment shown in this way is measured. The bank numbers of a few suitable grafts of this size [illegible] here, when needed, [illegible]. An estimate is [illegible] not easy, the site of the block, the build and sex of the patient and to some extent the arteriographic appearance should be taken into account. *Using freeze-dried or frozen storage* it is possible to keep a good selection of grafts from which a graft of the correct length and diameter can be chosen. It is often enough to substitute a femoral artery graft

for a femoral artery block, but in some cases, in which the recipient vessel has been much narrowed by disease, a brachial artery is more suitable; this particularly applies to the popliteal. It should be remembered that after thawing, frozen arteries are found to increase by about one-fifth in diameter. If when fresh the vessel size is judged to be slightly too small, on thawing the fit should be perfect, but if a graft is chosen whose diameter when fresh was slightly too large this discrepancy may prove troublesome in making the anastomosis. We have not attempted to use grafts in the order in which they were taken. Some have been in the bank for eighteen months awaiting a suitable case, others have been used within two weeks of collecting. The oldest graft so far used had been in store for eight months (Figs. 3 and 4); it measured 20 centimetres and is functioning well at the time of writing.

Operative technique

Anaesthesia

A light general anaesthetic is used, with intubation only if the prone position is needed.

Position

For lesions confined to the lower popliteal artery, in which it is certain that there is no involvement in the upper portion near the adductor foramen, the prone position

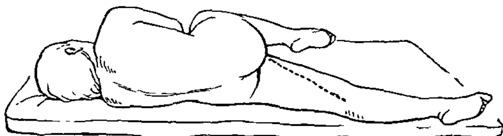


FIG 27.—Position used for the exposure of the superficial femoral and popliteal arteries.

is satisfactory. An arm is brought forward and is used for a continuous intravenous glucose saline infusion, for which blood may be substituted if necessary.

Where both the femoral and popliteal portions of the artery are affected the lateral position has been found to be very satisfactory (Fig. 27). With the patient on the affected side, the sound leg is flexed well forward, the operative site is relaxed by slight flexion of the knee using a sandbag under the dorsum of the foot. The whole operation can now be conducted with everyone concerned in it comfortably seated. We have found this position adequate for the exposure of the whole length of the superficial femoral and proximal two-thirds of the popliteal arteries.

Incision and exposure

A longitudinal incision is made along the course of the artery. The subcutaneous and deep fasciae are divided in the same line, care is taken not to cut across the internal saphenous vein as this part of it may be needed for the graft. At all stages of the operation the most scrupulous haemostasis is essential. Even with it the effect of heparin in causing reactionary bleeding can be very troublesome.

Few vessels require formal ligation before the vessel sheath is opened. Until this stage is reached diathermy cauterization of the small points suffices. It is usually found that very few arterial branches are encountered in the approach to the block.

Exposure can be improved by inserting a self-retaining retractor of the Mayo or Harvey Jackson type. The portion of the adductor magnus which lies superficial to the artery is divided It is often found to be compressing it by an aponeurotic band.

Mobilization of the artery

The pulsations which mark the upper limit of the block are easily felt. It is important to obtain an adequate exposure of the whole area from several centimetres proximal to an equal distance distal to the thrombosed segment. This is essential for adequate control of the ends of the recipient artery during the anastomosis. At

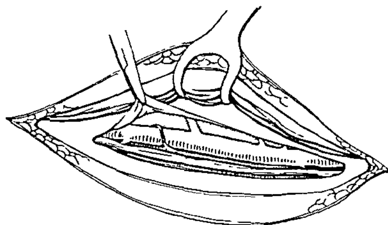


FIG. 28.—Opening the vascular sheath. Note the small vein crossing the artery and close relationship of the femoral nerve.

this stage collateral vessels are not divided but later, when a definite decision to graft has been made, it is better to divide collaterals and make a sound anastomosis than to temporize by preserving vessels which will interfere with the operation.

The patent portions of the artery beyond the block are easily dissected from the artery bed, but along the affected segment adhesions make it difficult to separate from the vein. It is very important to preserve the main vein because of the marked hyperaemia which follows a successful graft. Small venous tributaries which cross the

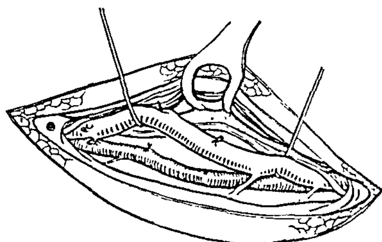


FIG. 29.—Artery mobilized. Vein preserved.

artery are ligated and divided (Figs. 28 and 29). Artery branches are preserved if [illegible] thrombosed [illegible] arrangement of the main artery occlusion is known.

The lower end

Finding and preparing this is the most difficult part of the operation. Whereas at the upper limit the pulsations in the main artery and in the collateral vessel leaving it

are easily seen and felt, below the block the artery is usually much thickened; though it contains blood there is seldom a pulse.

One method is to apply a Blalock's clamp or a tape tourniquet well below the suspected lower limit and to open the artery transversely with a knife in a hard portion of it near the suspected lower collateral. The block itself acts as the upper clamp, which therefore need not be applied until later.

Patent collaterals above the lower clamp or tourniquet will cause bleeding through the cut end once the continuous lumen has been reached. Unless this retrograde bleeding occurs, successive trial sections must be made down the artery until an adequate lumen is obtained. Small rubber-shod bulldog clamps are then placed on the lower collateral arteries (Fig. 30). When grafting arteriosclerotic vessels the host artery will be abnormal and atheromatous; this probably extends throughout the whole vessel. There is a tendency for the surgeon to feel that the next portion will be better than the one he can see. This temptation to go on removing the artery must

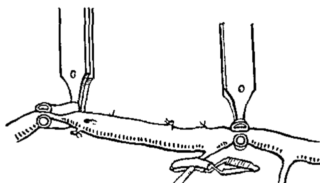


FIG 30.—Artery mobilized; bulldog clamp occluding a lower collateral.

be resisted and the anastomosis performed at the first place where an adequate lumen is found, even if one has to suture through a plaque of atheroma

The lower end of the recipient artery is often half occluded by organized thrombus and atheroma which is apt to flake away from the media Too hard an arterial clamp on this type of vessel will dislodge this inner layer which will then occlude the lumen. Loose flaps of it near the proposed line may be forced down and across the lumen when the blood is later allowed to flow through the graft For this reason we prefer a tape tourniquet to an arterial clamp. It is difficult to avoid loosening this tissue and almost impossible to suture it back into position again If it is removed a fresh separation may develop below, out of sight and reach.

Fortunately, many arteries are sclerosed in a different way More uniform thickening and closer fibrous adherence of this part of the wall to the true media provide a good end for anastomosing to the graft As soon as the clamps are in place for the insertion of the graft, heparin 12,500 units is given intravenously. This prevents spreading thrombosis beyond the clamps and later in the graft itself if the clamps need to be reapplied.

Preparation of the graft

As already described, a frozen graft is brought to the operating theatre in a special container of dry ice freezing mixture at a temperature of −79° C. When the surgeon has decided which graft he is going to use the tube is removed from the container and handed to him. The outside of this tube is not sterile and is very cold so we hold it in a thick sterile abdominal pack and remove the rubber stopper from the tube. The graft should be thawed as rapidly as possible by pouring sterile isotonic saline at blood heat, 37° C., into the tube, and then as soon as the graft is loose to tip it into a bowl of saline at the same temperature. Freeze-dried arteries are reconstituted by filling the tube with sterile isotonic saline. Rehydration is usually complete in less

than 30 minutes. When the graft is ready it is prepared by tying all branches with fine silk, if these were cut too short during removal from the donor it will be necessary to use a transfixion suture of fine silk. Lastly, the adventitia is stripped back and removed for a distance of one centimetre or so from the end to be anastomosed first (Fig. 31).

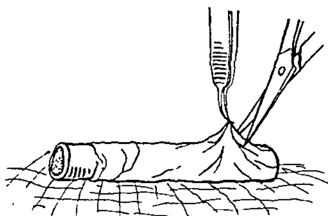


Fig. 31.—Adventitia being stripped back from the ends of the graft

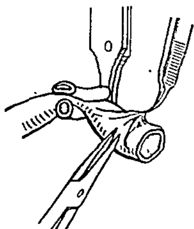


Fig. 32.—The vessels are held by adventitia; dissecting forceps should not be applied to the intima

If a vein graft is judged to be suitable, the saphenous vein is divided where it enters the lower end of the wound and the free end prepared by stripping one centimetre of adventitia from its end, ready for anastomosis to the pulsating upper stump of the femoral artery, the upper anastomosis in this case being performed first.

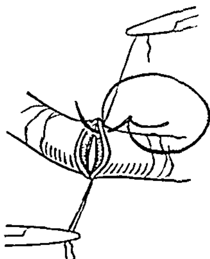


Fig. 33.—Two interrupted everting mattress stay sutures have been inserted

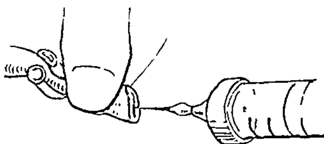


Fig. 34.—Injection of heparin solution into the lumen before the anastomosis is begun.

The lower anastomosis

The lower anastomosis is usually performed first; it is the more difficult of the two, and to be able to turn back the graft to place the posterior row of sutures is helpful. Another reason is that the upper end need be clamped for a shorter time if the blocked segment is left attached to it while the lower anastomosis is being performed. Strong pulsations under a clamp on this type of artery can be harmful to its diseased lining, therefore the time of clamping should be kept as short as possible.

The artery stump and the end of the graft are cleared of their adventitia (Fig. 32).

A pair of everting mattress sutures are placed on opposite sides of the proposed anastomosis (Fig. 33). A small quantity of heparin solution is placed within the lumen of the graft and in the open cuff of the host vessel (Fig. 34). The anterior half of the anastomosis is then inserted, using an everting mattress stitch (Fig. 35), preferably continuous since it is haemostatic. We use 00000 silk well lubricated with sterile paraffin. The posterior layer is then sutured in the same way but with the graft turned back (Fig. 36). It should be kept moist with isotonic saline during the whole operation. We have a 2·5 per cent solution of papaverine available for local application to the artery should spasm develop during the operation.

Cutting the graft to length

Arterial grafts must be inserted under enough tension to ensure that redundancy does not develop when the blood is allowed to flow through (Fig. 37 (*a*) and (*b*)). The graft should be cut at least 20 per cent shorter than the gap which is to be closed. This will often require a third soft clamp on the graft to help maintain apposition while the upper anastomosis is begun. The posterior half of this is best performed by rotating the graft and stump, if necessary after shifting the clamps, or if the upper clamp is placed high, simply by twisting the anastomosis with its stay sutures.

The lower clamp is now removed, and the graft fills with blood from below. Bleeding from leaks in the anastomosis or small unligated branches of the graft or the recipient artery may need to be controlled. Interrupted mattress stitches between the flanges of the arterial anastomosis quickly stop haemorrhage from this site. A suture or forceps ligature of fine silk or cotton is used for other bleeding points.

The upper clamp is removed and normally no further leaks develop, since the continuous sutures now tighten to their fullest extent.

Wound haemostasis and closure

A final search is made for bleeding points and to ensure that no small artery clamps or pieces of rubber tube used in the tape tourniquets remain. The skin is brought together at the centre of the wound only with a single stitch. This approximates the muscles to cover the graft but permits free drainage into a very thick sterile dressing which is then applied

The generalized post-operative oozing in heparinized patients will, if the wound is fully closed, infiltrate the muscle planes, clot, and produce a painful set swelling. Such a wound needs to be laid open because of tension; it may be many weeks before the swelling subsides and secondary closure can be performed. None of this difficulty is encountered if delayed primary suture is adopted as a routine.

Post-operative care

Heparin

After grafting a peripheral vessel for arteriosclerosis we heparinize the patient for 2–3 days. We do not think that heparin is necessary if the host vessels are normal and consider that it is both unnecessary and unsafe when larger vessels like the aorta are grafted. Sufficient heparin is given in the intravenous infusion to maintain the clotting time as measured by the capillary tube method at 15 minutes (Murray, 1941) The amount required to achieve this varies in different patients. A 4- or 6-hourly dosage of 5,000–10,000 units is usually sufficient. Continuous infusion of a dilute solution has been found to be more exacting in its demands on the resident medical and nursing staff than intermittent injection into the infusion tubing. Intramuscular injection, usually 15,000 units 8 hourly (Wynn, Goodwin and Birbeck, 1952) has also been used. These injections are sometimes very painful, and may produce a haematoma; to reverse their effect repeated doses of protamine sulphate (10 millilitres of 10 per cent

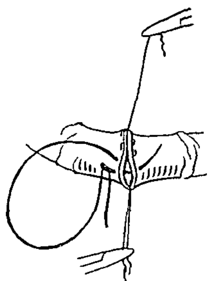


Fig. 35.—Anterior half of the lower (first) anastomosis with a continuous everting mattress stitch

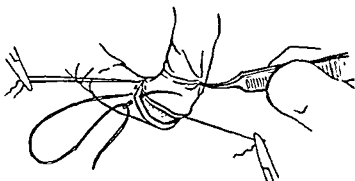
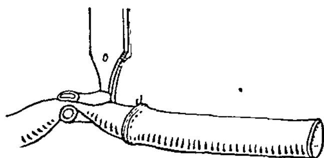
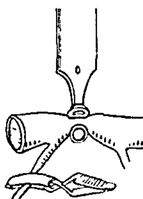
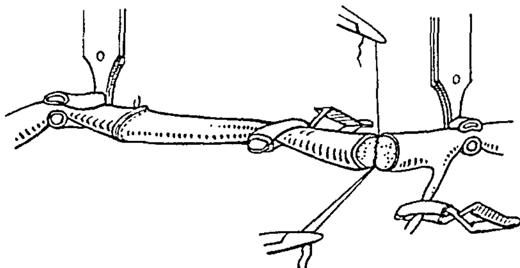


Fig. 36.—Posterior layer of lower (first) anastomosis with graft turned back.





(a)



(b)

Fig. 37 (a) and (b).—The second anastomosis should be made under tension.

solution intravenously) may be needed. On the other hand, it is possible to maintain a more uniform level of heparinization with this method than with the intermittent intravenous dosage, and perhaps for this reason a smaller overall dosage may be used.

Regional heparinization

The disadvantage of systemic anticoagulant therapy in vascular surgery has been the high incidence of haematoma formation in the immediate post-operative period. Murray and Best (1938) first suggested regional heparinization as a safer alternative. They recommended this method for use after a vascular anastomosis. As used today, a very fine polythene tube is inserted into the vessel and passed to the region of the anastomosis. A constant saline infusion containing about 200 milligrams (26,000 international units) of heparin daily is maintained for up to a week, after which the tube is withdrawn. It is claimed that this method prolongs the clotting time of the blood in the region of the anastomosis but has less effect on the systemic clotting time. This finding has never been proved; this dosage of heparin prolongs the clotting time of the systemic blood to 20 minutes or more and may produce a greater prolongation regionally, but in all published work this has been an assumption and not a proven fact. The idea, however, is attractive.

It has been our experience that in a patient with a large operation wound all forms of heparinization, even with the most rigid control, cause a high incidence of wound haematomas. For this reason we now leave these wounds open. The oozing blood escapes into dressings and not into the patient's tissues On the third day the heparin is stopped and on the fourth the wound is closed by the operation of delayed primary suture. Since adopting this method we have had no trouble from post-operative haematomas but we have needed to give more blood.

Pulse and blood pressure records

These findings should be recorded half hourly during heparinization. Transfusion should be sufficient to keep the systolic blood pressure approximately halfway between 100 millimetres of mercury and the normal reading The patient's posture is governed by the blood pressure readings. A satisfactory daily urine output is good evidence that an adequate level of blood pressure is being maintained

The foot pulses on the affected side are palpated at regular intervals. In our experience, if they are present on return from the operating theatre, they usually remain palpable. In other successful cases, however, they may not make their appearance until 24 hours after the operation

Drugs

Penicillin is given as a routine in view of the widely opened soft tissue wound, and is discontinued a few days after the delayed primary suture if the patient remains afebrile.

Morphine is seldom needed unless tension develops within the dressing. This should be loosened but not removed; the pain is usually relieved as a result. Reactive hyperaemia of the ankle and foot region may be intense and painful, needing analgesics.

Delayed primary suture

Delayed primary suture is performed in the theatre under general anaesthesia. By this time the heparin will have been discontinued and the intravenous infusions also.

The large pad of dressing containing the clotted drainage of the heparin period is removed and the leg is draped in the usual way.

Clots if present in the superficial part of the wound are scooped out, and the skin flaps are mobilized by blunt dissection with a finger. No attempt should be made to approach the graft itself. The clot which lies in the depths of the wound must not be disturbed.

Enough interrupted sutures are inserted to close the whole of the wound. Drainage is not necessary.

Active movements

With the new and lighter dressing and his wound closed the patient can begin to perform movements in bed in much the same form and rate of progress as is adopted after excision of the semilunar cartilage from the knee.

Weight-bearing and full active flexion are allowed from the tenth day, and the sutures are removed according to the appearance of the wound, normally on the tenth day after the delayed primary suture.

Post-operative arteriography

This is usually performed on the fourteenth day. It is particularly important in patients with reduced or doubtful pulsation below the graft. In one patient an acute thrombosis developed on the tenth day; immediate arteriography confirmed that the graft was blocked. The femoral artery was therefore exposed in Scarpa's triangle at the level of the upper limit of the graft. The host artery was opened below a tape tourniquet, and a fine polythene tube attached to the sucker was passed several times down the vessel and finally reached the lower limit of the graft. In this way the clot was removed and a patent channel restored. Retrograde bleeding then occurred. The arterectomy was repaired by suturing and heparin was recommenced. The pulses returned to the foot and subsequent arteriography showed a good result. No further thrombosis developed and the graft has functioned well. The same method was employed in another patient who experienced a sudden recurrence of symptoms seven months after a successful graft to the popliteal artery. Again, recent clot could be removed without difficulty, but there was an organized obstruction in the host vessel below the graft due to atheroma which prevented a retrograde flow except when dilated by the polythene tube. Such a recurrence may be an indication for a second resection and grafting if other conditions are favourable.

Complications

Mortality

Fatal complications are likely to develop only in the group of patients with established gangrene, for then the standard of fitness is lowered. Claudication may mask a coronary insufficiency and others (Julian and his colleagues, 1952; Cockett, 1952) have reported deaths from this cause in the post-operative period; Cockett's case had a patent graft at autopsy. In our series one patient died six weeks later after an unsuccessful graft for established gangrene of the foot. His case history is given as the fourth patient under the heading "Failure of the Operation".

Morbidity

In elderly patients with threatened gangrene any of the usual post-operative complications may develop. Retention of urine is a particularly serious one.

Anaemia

A surprisingly low level of haemoglobin may be reached during heparinization with its steady blood and plasma loss from the open wound. Further transfusions and iron, preferably intravenously, are indicated.

Haemorrhage

Haemorrhage from the graft or the anastomosis is rare. Its control in the limbs is not difficult but in the body cavity bleeding from the reconstruction is likely to prove fatal unless quickly recognized and checked.

Superficial wound infection

This occurs in about 20 per cent of patients after delayed primary suture. It seldom delays the patient's discharge from hospital.

Results

Failure of the operation

If the operation fails this is most likely to be due to thrombosis soon after operation. Heparin is discontinued if the blockage is thought from the findings at operation to be due to atheromatous tissue. A delayed failure should be investigated as described above. In our experience failure has not led to loss of the limb unless gangrene was established before the operation. This is a very important point because failure has not made our patients worse in spite of division of some collaterals. The following are brief case histories of our failures, four patients in whom the grafts have thrombosed.

(1) *Mr. C. L. Aged* 47 *years. Chef*—Intermittent claudication right calf for nine months. Feet warm. No pain at rest Pre-operative arteriogram complete occlusion at level of adductor foramen extending downwards for 10 centimetres. Partial filling of the portion of the popliteal artery between the femoral condyles Foot blood flow.

Operation. Insertion of frozen popliteal artery homograft Two medium-sized collaterals divided at upper level of block Extensive friable atheroma at lower end. Disobliteration of lower stump necessary. Pulses never returned to foot although graft functioned normally on removal of clamps

Post-operative arteriogram. Main flow now through profunda femoris collaterals Thrombosis of femoral artery has extended 10 centimetres higher. Good filling of lower end of popliteal artery and the calf vessels

Right foot: condition unchanged

Blood flow: not changed.

Exercise tolerance: not changed.

(2) *Mr. H. P. Aged* 47 *years. Machinist.*—Severe intermittent claudication left calf and thigh for two years Sudden onset with cold leg Left lumbar sympathectomy at Colchester. Nutrition of leg much improved Claudication remained

Aortogram. Occlusion of external iliac artery at inguinal ligament; faint filling of superficial femoral artery in femoral triangle.

Operation. Sixteen centimetres of frozen arterial homograft inserted. *No heparin* given Immediate failure—probably thrombosis in graft while temporarily occluded during the operation.

Post-operative aortogram: no change.

Plethysmography not performed.

Exercise tolerance: unchanged.

2nd Operation 9 months later. The thrombosis was found to have spread up to the bifurcation of the common iliac artery and halfway down the superficial femoral artery No graft sufficiently long was available. A long dissection of saphenous vein in the normal leg was not considered justifiable.

Exercise tolerance: unchanged.

Waiting for a suitable graft for a third attempt.

(3) *Mr. F. Aged* 76 *years. Retired.*—Diabetes. Claudication both calves for two years Dry necrosis of right fourth toe one year ago. Referred to authors with established wet gangrene of left forefoot.

Pre-operative arteriogram. Lower femoral artery occluded, popliteal and calf vessels failed to fill.



Fig 38



Fig. 39

Figs. 38 and 39 —Pre-operative and post-operative aortograms showing thrombosis of a common and external iliac graft.



Fig 40



Fig 41

Figs. 40 and 41.—Thrombosed popliteal artery and successful artery graft, October 1951.

Operation. Exposure of 16-centimetre block, much of it recent. Graft of frozen artery inserted. Wound infection. Graft thrombosed.

Amputation performed on tenth day, at level considered necessary before attempted reconstruction. Patient later developed prostatic retention of urine and died of pyelonephritis with uraemia.

(4) *Miss C. Aged* 37 *years. Secretary.*—Sudden onset of claudication in right calf two years before. Limit 200 yds. A year later, sudden pallor of foot which had since been painful and blue on dependency. Walked only a little. Amputation considered. Referred in view of this.

Pre-operative aortogram (Fig. 38) Complete occlusion of right common, external and internal iliac arteries.

Operation. Excision of external iliac, proximal part of internal iliac, and lower half of common iliac arteries Disobliteration of remaining stump of common iliac. Frozen brachial artery homograft inserted. Deep epigastric and circumflex iliac collaterals preserved. Heparin given for first 24 hours after operation

Post-operative arteriogram (Fig. 39) No change. Condition of foot much improved both subjectively and on examination. Exercise tolerance much increased (from 5 to 300 yds.). Improvement maintained 12 months later.

Successes

To date seventeen frozen or freeze-dried arterial homografts and a number of autogenous vein grafts have been inserted with good immediate results. The histories of these will not be given in detail but most have been reported by Eastcott (1953). The case history of one patient of particular interest will, however, be reported in full.

Mr. E. C. Aged 58 *years. Milk roundsman.—July* 1951 *Onset of intermittent claudication* left calf Pulses absent below groin on left, all palpable on right.

Arteriography August 1951 (Fig. 40) showed localized popliteal artery thrombosis with diffuse arteriosclerosis.

October 1951 *operation.* Excision of 8-centimetre block extending downwards from adductor foramen Reconstruction with frozen arterial homograft.

Arteriography fourteenth day (Fig. 41) showed graft functioning Pulses remained normal in the affected foot which had become hyperaemic and rather painful shortly after operation. Steadily regained full activity and could run.

January 1952 returned to work.

August 1952 patient developed a complete recurrence of symptoms with loss of distal pulses on left side and pain at rest in the foot. Early gangrene developed in the great toe and amputation was considered.

Arteriography (Fig 42). Fresh occlusion at the level of a large plaque seen in the previous film, a short distance above the upper end of the graft

Left lumbar sympathectomy August 1952 produced no change in rest pain; foot and lower calf still cool.

Operation September 1952 Recent thrombus in superficial femoral artery above graft, the lower portion of which was patent Twenty centimetres of femoral and previous graft resected, and frozen homograft stored for eight months inserted (Fig. 44).

Immediate return of pulses Hyperaemia of foot soon developed. On tenth day, during a blood transfusion, the patient experienced a sharp pain in the leg, which quickly cooled; its pulses could not be felt Arteriograms showed a recurrence of thrombosis. Since this was fresh, and it was known that no structural stenosis was present, the femoral artery was exposed through a short incision in Scarpa's triangle and the upper limit of the obstruction was located. Through a one-centimetre incision the soft clot was removed using a medium-sized polythene suction tube, 30 centimetres long This was finally passed down to the popliteal artery below the graft, clots ceased to appear, retrograde bleeding took their place The arterial incision was repaired and the patient was heparinized.

Arteriogram on discharge from hospital showed a good result (Fig. 43). The toe and foot quickly recovered, and its pulses have been palpable ever since. Fig. 45 is a microphotograph of the original graft stained for elastic fibres.

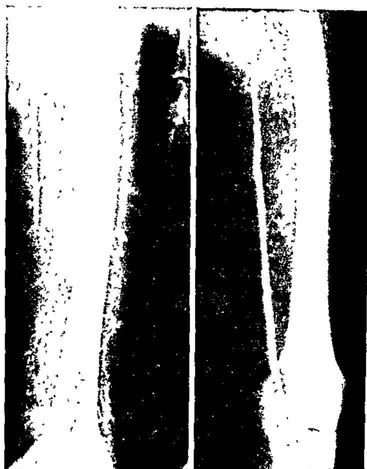


Fig. 42.—Complete recurrence of symptoms Arteriogram shows a fresh thrombosis, August 1952.

Fig. 43.—Post - operative arteriogram shows new graft in position.

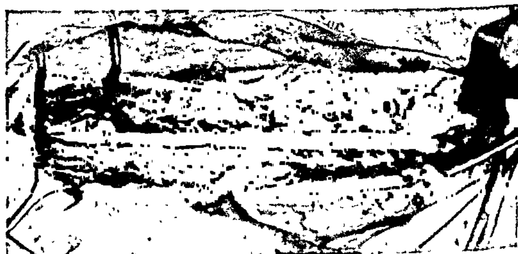


Fig. 44.—Area of previous graft and fresh thrombosis exposed. Graft found to be patent; fresh thrombosis was in host vessel proximal to it. New graft inserted

This patient is now maintained on long-term anticoagulant therapy with dicoumarin. This is less difficult to stabilize than Tromexan. Prothrombin estimations are performed once or twice weekly. The maintenance dose in this case is between 50 and 75 milligrams daily. He is now able to undertake full activity once more

CONCLUSION

In conclusion we wish to stress what we think are the two most important aspects of arterial grafting: the selection of patients for this operation, a warning about arterial grafting in patients with arteriosclerosis (and a few remarks about the future of this branch of vascular surgery). We would also like to put on record that the first human frozen artery bank to be installed in the world is functioning at St Mary's Hospital, London, and for this we owe Charles Hufnagel a great debt. He is also largely responsible for our change-over to the improved technique of freeze-drying.

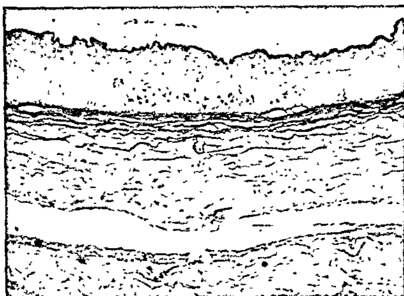


Fig 45.—Microphotograph of the graft which had been in position for 11 months Note elastic fibres and thick intima.

The selection of patients for grafting

Certain indications for this operation are obvious and need not be elaborated further. Under this heading we include a coarctation of the aorta which cannot be repaired by direct suture, an aneurysm of a major vessel which is causing symptoms, war wounds and civilian injuries, and certain locally invasive malignant neoplasms. In these patients the decision is whether to use an autogenous vein graft or a homologous artery graft; this has been discussed We favour vein grafts when the host vessel is normal or nearly so, and arterial grafts for all defects of the aorta, its major branches and patients in whom the host vessels are arteriosclerotic.

In the case of patients with arteriosclerosis the decision to graft is less obvious and a successful graft, although producing local improvement, may do harm to the patient as a whole. We believe that patients with "primary thrombosis" of a main artery (Figs. 15 and 16), such as the popliteal, are suitable for grafting; it is rare for these patients to have evidence of generalized arterial disease For patients with true arteriosclerosis the strictest criteria for selection must be adopted. Surgery can benefit the local manifestations of this general disease only if these predominate to

an unusual extent. For the symptom of intermittent claudication we apply very strict selection, about 60 per cent of such patients have a lesion which is anatomically suitable for a graft, but in our opinion less than 20 per cent of these should be grafted (Rob, 1953a). For early gangrene when the alternative is a major amputation we advise grafting wherever the arterial lesion is anatomically suitable. From the patient's point of view a graft is a less severe operation than a major amputation and if successful the ischaemic tissues may heal or local surgery may become possible.

A warning

Atheroma, calcification and aneurysm formation have not occurred to date in frozen arterial grafts. They have been reported in frozen and irradiated grafts (Hui and his colleagues, 1952) but these had not been used in man. In our opinion this is not the danger. The danger is the indiscriminate grafting in patients with arteriosclerosis; these patients tend to thrombose their arteries. Without careful selection successful grafts will be followed by many deaths from coronary or cerebrovascular occlusion, or recurrence of symptoms due to thrombosis of the arteries of the other limb or the host vessels of the grafted limb. In our experience the grafts usually remain patent even if the adjacent host vessels thrombose.

The future of arterial grafting

We have in this paper discussed the reconstruction of arteries down to the size of the human popliteal or brachial. In the future we may be grafting smaller vessels such as the coronary arteries. The main stems of human coronary arteries are larger than a dog's common carotid which is about 3 millimetres in diameter and a dog's carotid graft remains patent in about 75 per cent of cases (Eastcott and Hufnagel, 1950). The human heart beats in such a way that the main stems of the coronary arteries are relatively still and it should be possible to graft them with the heart beating. Murray (1950) has replaced a segment of a dog's coronary artery with a vein graft. The difficulty here will be the selection of patients. This problem is being studied and it is possible that a few patients with angina pectoris and coronary occlusion may have a lesion in their coronary arteries which will be suitable for replacement with a graft (Rob, 1953b). The ideal patient should have normal vessels apart from an occlusion of the main stem of one coronary artery.

The cerebral arteries also may be grafted within the next few years. They are thin-walled and the operation will be technically difficult but by no means impossible. The highly developed state of cerebral arteriography should make the selection of patients relatively simple. Perhaps coronary arteriography through a catheter introduced *via* an artery into the aorta may be developed to assist in the selection of this group of patients as well.

Lastly, the aorta has been grafted between the left subclavian and the diaphragm, and below the renal arteries. This leaves untouched the ascending aorta, the arch of the aorta and the upper abdominal aorta. Occasionally, an aneurysm in these locations threatens life sufficiently to warrant major surgery. The difficulties of grafting will include not only the multiple anastomoses, but, more important, the necessity for maintaining a blood flow to such vital structures as the brain, spinal cord and kidneys. It may be possible to overcome this latter difficulty by performing the anastomosis over plastic tubes (Hardin, Batchelder and Schafer, 1952) which would transmit the blood during the operation; just before the completion of the final anastomosis these would be removed, and previously inserted stitches tied.

(*See also British Surgical Practice* Arteries, Vol 1, page 327, S. Key 37)

REFERENCES

Bazy, L., Huguier, J., Reboul, H., and Laubry, P (1947). *Mém. Acad. Chir.*, **73**, 602.
— (1949). *J. Chir.*, **65**, 196.
Berman, J. K., and Hull, J. E. (1952) *Surg Gynec. Obstet*, **94**, 543.
Blakemore, A. H., Lord, J. W., and Stefko, P. L. (1942) *Surgery*, **12**, 488.
Boyd, A. M., Ratcliffe, A. H., Jepson, R. P., and James, G. W. H (1949) *J. Bone Jt. Surg.*, **31B**, 325.
Brock, R C. (1952). *Trans. med. Soc. Lond*, **68**, 216.
— (1953) *Proc R. Soc. Med*, **46**, 115
Carrel, A. (1908). *J Amer med Ass*, **51**, 1662
Cockett, F. B (1952). Personal communication.
Cohen, S. M. (1952). *Ann R. Coll. Surg Engl*, **11**, 1
Donovan, T. J, Hufnagel, C. A., and Eastcott, H H G. (1952) *J thorac Surg*, **23**, 348.
Dubost, C., Allery, M., and Oeconomos, N. (1951) *Arch Mal Coeur*, **44**, 848
Eastcott, H. H. G, and Hufnagel, C. A (1950). American College of Surgeons, Surgical Forum, p. 269.
— (1953). *Ann. R. Coll. Surg. Engl* (In press)
Eden, K. C. (1939). *Brit J. Surg.*, **27**, 111
Edwards, E. A., and Levine, H. D (1952) *New Engl. J. Med*, **247**, 79
Fontaine, R., and Hubinot, J. (1950). *Acta chir belg.*, **49**, 580
— Buck, P., Riveaux, R., Kim, M., and Hubinot, J (1951). *Lyon chir.*, **46**, 73.
— Riveaux, R., Kim, M., and Kiey, R. (1952) Proc. Cong, European Cardio-Vascular Surgical Society, p. 227.
Forty, F. (1952). *Brit. med. J*, **2**, 264.
Freeman, N. E., and Gilfillan, R. S. (1952) *Surgery*, **31**, 115
Gerbode, F, Holman, E, Dickenson, E. H., and Spencer, F C (1952) *Surgery*, **32**, 259.
Griffiths, D. L. L. (1940) *Brit. J. Surg*, **28**, 239
Gross, R. E., Bill, A. H, Peirce, E C (1949) *Surg Gynec Obstet.*, **88**, 689
Halsted, W. S (1912) *Johns Hopk. Hosp Bull*, **23**, 191
Hamilton, M, and Wilson, G M (1952) *Quart J Med*, **21**, 169
Hanks, J. H, and Wallace, R E. (1949) *Proc Soc exp Biol, N Y*, **71**, 196.
Hardin, C. A., Batchelder, T. L, and Schafer, P W (1952) *Surgery*, **32**, 219.
Hufnagel, C. A., and Eastcott, H H G. (1952) *Lancet*, **1**, 531
— (1953). Personal communication.
Huguier, J. (1948) *Pr méd*, **56**, 560B
Hui, K. K. L., Keefer, E. B C., Deterling, R A, Parshley, M S, Humphreys, G H, and Glenn, F. (1952). American College of Surgeons, Surgical Forum, p 255
Hume, D M., Merrill, J. P, and Miller, B F. (1952) American College of Surgeons, Surgical Forum
Hurwitt, E S, and Kantrowitz, A (1952) *Surgery*, **32**, 76.
Hyatt, G. W., Strong, W. R., Pate, J. W, and Evans, V J. (1953) Personal communication.
Johnson, J., Kirby, C. K., Greifenstein, F E, and Castillo, A. (1949) *Surgery*, **26**, 945.
Julian, O. C, Dye, W S, Olwin, J. H, and Jordan, P H (1952) *Ann Surg*, **136**, 459.
Kekwick, A (1951) *Proc. R Soc Med*, **44**, 983
— McDonald, L., and Semple, R (1952) *Quart J Med*, **21**, 185
Kinmonth, J. B (1952). *Brit. med J*, **1**, 59.
Kunlin, J (1948). *Mem Acad. Chir*, **74**, 553.
— (1949). *Arch Mal. Coeur*, **42**, 371.
Learmonth, J. R., Blackwood, W, and Richards, R L (1944) *Edinb med. J*, **51**, 1
— and Slessor, A J. (1952). *Brit med Bull*, **8**, 375.
Leriche, R., and Kunlin, J (1947) *Lyon chir*, **42**, 675
Lewis, T., and Grant, R (1925) *Heart*, **12**, 73
— and Pickering, G W (1934) *Clin Sci.*, **1**, 327
Lexer, E (1912) *Verh dtsch Ges Chir*, **41**, 132
Linton, R R. (1951) *Angiology*, **2**, 485
Lynn, R. B, and Barcroft, H (1950) *Lancet*, **1**, 1105
Macpherson, A I. S, Nabatoff, R. A., Deterling, R A., and Blakemore, A H. (1951) *Arch. Surg.* **63**, 152
Makins, G. H. (1919). *Gun Shot Wounds of Blood Vessels*, p 95 Bristol; Wright.
Marrangoni, A. G., and Cecchini, L. P. (1951) *Ann Surg*, **134**, 977.
Martin, P. (1952) Personal communication.
— and Lynn, R B. (1952) *Brit. J. Surg*, **39**, 352
Mason Brown, J. J. (1946) *Proc R. Soc. Med*, **39**, 483

Maybury, B. C. (1944). *Brit. med. Bull*, 2, 142.
McCune, W. S., and Blades, B (1951). *Ann. Surg.*, 134, 769.
Meeker, I. A., and Gross, R. E (1951). *Science*, 114, 283.
Mowlem, R. (1941). *Brit. J. Surg.*, 29, 182.
Murray, G. D. W. (1939) *Brit J. Surg.*, 27, 567.
— (1941). *Surg. Gynec Obstet.*, 72, 340.
— (1950). *British Surgical Practice*, Vol. 8, p. 524. Butterworth; London.
— and Best, C. H. (1938). *Ann Surg.*, 108, 163.
Peirce, E. C. (1952). *Ann. Surg*, 136, 228.
Pickering, G. W. (1933) *Brit med J.*, 2, 1106.
Reboul, H., and Huguier, J. (1949). *Mém Acad. Chir.*, 75, 318.
— and Laubry, P (1950). *Proc. R. Soc. Med*, 43, 547.
Reid, S. F., and McKenzie, A. (1952). *Aust. N. Z. J. Surg.*, 21, 269.
Rob, C. G. (1953a). *Proc. R. Soc. Med*, 46, 121.
— (1953b) *Brit. med. J.*, 2, 308.
Rokitansky, C. (1852) *Manual of Path. Anat*, 4, New Sydenham Soc., 262.
dos Santos, J. C (1947). *Mém. Acad Chir.*, 73, 409.
Seeley, S. F., Hughes, C W., Cook, F. N , and Elkin, D. C. (1952). *Amer. J. Surg.*, 83, 471.
Shepherd, J. T. (1950) *Clin. Sci.*, 9, 49.
[illegible] 101
[illegible]), 568.
[illegible]

POST-OPERATIVE BRACHIAL PLEXUS PARALYSIS

By M. R. EWING, M.B., Ch.B., F.R C.S.
Senior Lecturer, Postgraduate Medical School of London

INTRODUCTION

Considerable attention was given at the turn of this century to the not infrequent occurrence after surgical operations of paralyses in the upper extremity. Büdinger in 1894 reported nine cases from Billroth's clinic in Vienna and believed it to be quite common in the practice of his surgical colleagues This was followed by several contributions in the American literature (including an excellent presentation read by Garriques in 1897) and a paper on this subject was read by Turney to a meeting of the Society of Anaesthetists in London in 1899 By 1903, Cotton and Allen were able to trace in the literature 30 reports of this complication, a number which they believed to bear no very close relationship to its true frequency.

Although at first attributed—and perhaps not unnaturally—to the use of the new and largely untried anaesthetic agents, it soon became convincingly established that the paralysis was determined in almost every instance by the positioning of the patient on the operating table.

The prominence given at this time to this unfortunate happening may have led to steps being taken in its avoidance, for the subject has, until recent years, since received but scant attention in the literature. There is, however, every indication that these injuries are once again being encountered in every branch of surgical practice with a disturbingly high frequency (Clausen, 1942, Pommerenke and Risteen, 1944; Slocum, O'Neal and Allen, 1948; Sinclair, 1948, Ewing, 1950; Kiloh, 1950; Raffan, 1950; and Wood-Smith, 1952a). Despite the potential seriousness of this post-operative complication, it has not yet been given the publicity which it seems to deserve. It is certainly true that, of all the postural nerve injuries which follow operation, those of the brachial plexus are the most frequent as well as the most disabling.

EXTENT OF THE PARALYSIS

The lesser paralyses

It seems highly probable that minor injuries to the plexus often pass unnoticed. No doubt a slight weakness of the elbow or wrist is, in the first few days after operation, often attributed by a patient to some unavoidable effect of the operation, and is as readily overlooked by his medical attendant. It is, for example, not uncommon for a patient in the immediate post-operative period to find that he is unable readily to lift a full tumbler from his bedside table, to manipulate his razor with precision, or even to grip a pen. He may make no complaint while he is in hospital and these symptoms are elicited only later when, at the follow-up clinic, he is found to have weakness of the elbow flexors and is first noticed to have some wasting and flaccidity of the biceps. Awareness of the risk of damage to the plexus, especially during the course of long operations in certain positions, soon leads, however, to an earlier clinical recognition of these lesser paralyses and to an appreciation of their true frequency.

The major injuries to the plexus cannot, however, readily be overlooked; from the outset they cause considerable disability.

Partial paralysis

Distribution

Most commonly there is a partial paralysis of the plexus or of its main divisions. It is the upper components which suffer most often and most severely, the brunt of the injury being taken by C.5 and 6. The distribution of the paralysis conforms in the great majority of cases more or less to the Erb-Duchenne type, with weakness of the abductors of the shoulder and of the elbow flexors and supinators of the wrist. Paralysis of the deltoid, biceps, brachialis and brachioradialis is the commonest finding on clinical examination. Less often the lower part of the plexus is principally involved, with resulting loss of power in the small muscles of the hand.

Not infrequently, however, the whole limb is left limp and useless, indicating widespread damage to every component of the plexus. There is seldom evidence of damage to the plexus at root level. The diaphragm, rhomboids and serratus anterior will usually be found to have escaped; in injuries to the lower components of the plexus a Horner's syndrome is occasionally in evidence.

Degree

The paralysis is widely variable not only in its distribution but in its degree, being complete in some muscle groups while in others there is no more than a just detectable loss of power when compared with the opposite side. In one patient there may be serious crippling, in another no more than an irritating clumsiness and uncertainty in the execution of certain movements of the hand or forearm.

The paralysis may be bilateral, being often complete on one side and partial on the other. The simultaneous loss of motor function in each upper extremity is a major surgical disaster It occasions the most acute mental distress to a patient who, on recovering from his anaesthetic, finds that he is completely dependent on others not only to be fed and to move his position in bed, but for the most trivial needs of his personal toilet and even for the support of a newspaper.

Sensory dysfunction

The paralysis tends, in most instances, to be predominantly motor in type. In the less frequent injuries of the lower components of the plexus there may be loss of sensation along the medial margin of the forearm and in the hand, but it is uncommon to find any considerable evidence of sensory dysfunction in the commoner upper plexus lesions There is often, in the latter cases, a complaint of paraesthesia and, at the very outset, some dulling of sensation usually along the radial aspect of the forearm, but complete anaesthesia in even a restricted area of skin is distinctly unusual.

Pain

Surprisingly enough pain is seldom a prominent feature, even in the immediate post-operative period. Patients do, however, sometimes complain of aching discomfort in the root of the neck or across the shoulder, and tenderness is infrequently elicited by firm pressure immediately over the plexus on the affected side.

ASSOCIATED INJURIES

It is interesting to note that although the plexus is closely related, both in the root of the neck and in the axilla, to the main vessels, and although combined vascular and neurological symptoms seem so often to feature in the "costo-clavicular

syndrome", the blood-vessels do not in this condition often suffer any significant injury. Certainly "effort thrombosis" of the axillary vein is not a post-operative sequel in these cases, nor do we find any evidence of interference with the free flow of arterial blood. That the vessels are subjected, along with the nerves, to a variety of strains seems almost certain to be the case; their apparent immunity is attributable, no doubt, to their natural laxity and resilience, in contrast to the fixed and relatively unyielding and inelastic qualities of the main nerve trunks. It is sometimes noticed at operation that the radial pulse in an abducted arm has disappeared, while that on the other side remains quite unaltered. Alteration in the position of the arm, for example, by adduction or by raising the outer end of the supporting arm board and so correcting over-extension at the shoulder, will often cause its speedy reappearance. It is common experience too that the venous return in the abducted position may similarly be impeded, as indicated by a stoppage of the flow of an intravenous infusion (Galley, 1950).

NATURE OF OPERATION

Damage to the plexus has, in the past at least, been encountered most frequently in gynaecological practice. There is, however, no evidence to suggest that its high incidence in this speciality is in any way related to any peculiar vulnerability of the female sex in this respect. It is met with after any abdominal operation on the pelvic organs; of these hysterectomy is probably the most frequent, but paralysis is also encountered—and increasingly so in more recent times—as a sequel to resections of the distal colon and rectum or of the bladder

Probably next in frequency as a precipitating cause come operations on the biliary tract.

A significantly high proportion of the cases reported has occurred in the course of thoracic operations, or alternatively, following radical mastectomy. The factor common to these two types of operation is, no doubt, the not dissimilar positioning of the arm in relation to the trunk.

Injuries to the plexus have been reported following a wide variety of operations on the abdomen, and more especially after those which are complicated and exacting. They have similarly been reported following some of the more formidable orthopaedic procedures, such as hip arthroplasty. Even comparatively trivial operations are by no means immune, and paralysis has been reported following the straightforward incision of an axillary abscess

It is significant that this complication is rarely, if ever, seen following operations on structures situated above the level of the clavicle.

ANAESTHETIC

In the earliest descriptions of post-operative brachial plexus paralyses it is clear that they were regarded as being attributable primarily to the toxic action of the new narcotic agents: they were accordingly called "anaesthetic" paralyses. It is, however, now clearly established that none of the volatile anaesthetics has any lasting effect on the conductivity of the peripheral nervous system. It seems more reasonable to attribute the apparent marked increase in the frequency of this complication at that time not to the introduction of general anaesthesia into surgical practice, but to the more formidable operative procedures which their use made possible and that too under conditions of comparative leisure

The same argument might also be used with justification to explain the increase in the incidence of paralysis of this type in the years since World War II, an increase which has seemed, in time, closely to correspond to the widespread introduction into

anaesthetic practice of the use of the muscle-relaxant drugs. Consideration of the possible mechanisms of plexus injuries (*see* page 50) certainly *suggests that their* use involves a special hazard to the main nerve trunks at the root of the neck, but it must be freely admitted that few major operations—at least on the abdomen—are now carried to completion without the help of *one or other of the curare-like* substances. It is also true that there have been other changes in anaesthetic fashion which may be no less responsible. Chief among these is the recourse to the use of [illegible] *these days who do not*, at some stage or another during a surgical operation, bring the arm out into abduction for the administration of an intravenous anaesthetic. It is equally true that continuous venoclysis for resuscitative measures is a feature of many of the more extensive operations, and arm veins are all too commonly made use of for this purpose. We shall comment later on the harm which follows placing the arm in the abducted position.

There can be no question that general anaesthesia is important in the aetiology of these post-operative arm paralyses. They do not occur in the conscious patient, and it is also significant that there is no recorded instance following the use of a spinal anaesthetic. It is almost certainly true that it is the depth of the anaesthesia which *really matters; the immunity of neurosurgical operations from this complication* is no doubt directly related to the minimal muscular relaxation which their completion requires.

LENGTH OF OPERATION

As might reasonably be expected, the risk of paralysis is directly related to the length of the operation. In most of the recorded cases its duration has been two hours or thereabouts, but injury has followed an anaesthetic for the application of forceps lasting only 15 minutes. That length of operation is not significant *per se* is indicated by the rarity of paralyses following long neurosurgical procedures or time-consuming *resections of malignant disease in the mouth or neck.*

POSITION ON THE TABLE

It seems to be clearly established that one must look for the cause of the great majority of these plexus injuries in the positioning of the patient while under general *anaesthesia. In a few rare instances only they may be* directly attributable to manipulations of the arm during the course of an operation, for example, following sustained distraction of the arm at the shoulder, while demonstrating the capsular defect *in* a Bankhart operation. *Paralysis may also follow a high thoracoplasty*, and here, too, such a happening is usually the result of direct operative trauma to the plexus. Cotton and Allen (1903) maintained that no case of brachial plexus paralysis *had been recorded when the arm was carefully padded and tucked down* by the side or folded and supported in a relaxed position across the front of the chest. Although this is no longer strictly true, damage to the plexus with the arm in this *position is certainly a rare happening.*

Most frequently the paralysis is a sequel to an operation completed in the Trendelenburg position of a varying degree of steepness, the patient being *prevented from falling* by the support of shoulder rests, by the pressure of the calves against the dropped end of the table, or, rarely nowadays, by the securing of the wrists by leather cuffs fixed to the side of the table.

An additional hazard to the plexus is introduced when, with the patient in the head-down position and the shoulder firmly engaged against the rests, the arm is

brought out into abduction (Fig. 46), especially as the angle between the arm and the trunk reaches to and exceeds 90°. Even when the position of the arm is carefully adjusted in mild abduction at the outset, it will often be found to change considerably during the conduct of a long operation; in this respect alteration of the patient's position on the table is one of the greatest hazards, but pressure against the arm by eager assistants, or by spectators, or the further manipulations of the anaesthetist are no less serious.

Paralysis may also occur even when the patient is horizontally disposed and supine, when the arm is abducted. This is especially the case when the arm is secured back to an arm-board, tucked, as is so commonly the practice, under the rubber operating table mattress. To abduction is now added extension at the shoulder, and

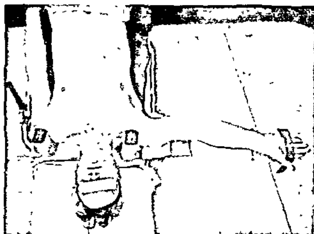


Fig 46 —Patient in steep Trendelenburg position with rests fitted and the shoulder in 90° abduction and lateral rotation, the elbow being extended and the hand fully supinated The plexus is, in this position, very liable to injury.

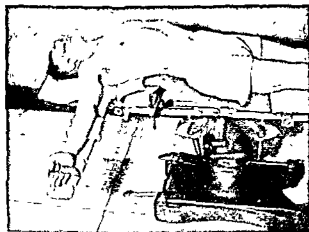


Fig 47 —Shoulder abducted to 90° and the arm secured back in extension to a board inserted under the rubber table mattress. The degree of extension at the shoulder is increased by the raising of the gall-bladder rest.

experience suggests that this new element in the position still further increases the risk to the plexus.

The degree of extension at the joint may be still further increased by throwing the chest forwards by a gall-bladder bridge, wedge or air cushion, during the conduct of a biliary operation (Fig. 47). With a gall-bladder operation-table bridge in position it is never easy to bring the arm down by the side for fear of an ulnar or radial paresis—from direct pressure against the metal support—and to leave them in flexion across the chest is equally inconvenient. The surgeon is tempted to put them well out of the way by pulling them out into the abducted position secured to an arm-board. This position is, next to the Trendelenburg tilt with the arm in abduction, the most dangerous.

Simultaneous abduction of each upper extremity is also commonly associated with

post-operative plexus paralysis, the more so if the arms are secured to a double arm-board in the "crucifix" position. Bilateral abduction is especially hazardous in the presence of a Trendelenburg tilt with shoulder rests in position or with a gall-bladder bridge raised as is not uncommonly directed in standard text-books on operative surgery. Thoughtless adduction of the limb on one side may then cause a dangerous degree of abduction of the opposite member.

In the records of post-operative paralysis *in the upper extremity at the beginning* of this century, the position of the arms during anaesthesia was often reported to have been that of simultaneous full abduction (hyperabduction) (Cotton and Allen, 1903). This was obviously the current practice in the early days of general anaesthesia, the elbows being folded and the forearms crossed on the pillow above the head (*Fig. 48*). *Although this position is seldom employed today,* full abduction of the left arm with the patient lying flat on his back is infrequently required during operations on the heart or great vessels or on the mediastinum. Abduction, but usually of a



Fig 48 —Arms brought up into hyperabduction by the side of the head. It is now uncommon practice for both arms to be fixed in this way simultaneously



Fig 49 —Patient in the lateral position with the uppermost arm in hyperabduction.

rather less severe degree, may also occasionally be instituted in order to give easy access to the axilla, as, for example, in a radical mastectomy, or in the axillary approach to the *cervico-dorsal sympathetic chain (Sellors, 1950).*

Lateral recumbency with the uppermost arm brought up in full abduction (Fig. 49) or alternatively up by the side of the face suspended from the anaesthetist's screen is also dangerous, and plexus paralysis has been noted after thoracotomy on patients in this position (Sweet, 1950) More commonly, during exploration of the chest, the patient lies half over on his face *with the uppermost arm drawn forwards* rather than upwards and directed downwards over the side of the table. This position, too, is not entirely without risk to the plexus.

Paralysis has also been found to follow operations in the complete prone position ... one of the easiest ways of disposing of the arms ... *on at the shoulder,* with ... ead. It is the placing of the arms in this position which causes the plexus injury.

Abduction of the arm would seem, therefore, to be one of the most significant factors in determining brachial plexus paralysis. Unfortunately, this is just the position of the arm which the anaesthetist tends to find the most convenient. It is no doubt significant that it is often the arm with the intravenous drip which comes to harm, or alternatively, when the paralysis is bilateral, it is this limb which is most seriously affected. The risk of abduction, or of the more serious abduction coupled with extension (that is to say, retraction) of the shoulder, is heightened still further when, with the elbow in extension and the forearm in full supination, the whole arm is externally rotated at the gleno-humeral joint. This is all too frequently the position in which the arm is secured when access is sought in a fat or in a shocked subject to the more prominent veins in the cubital fossa.

The position of the head in relation to the trunk is also important in determining the occurrence of paralysis. Hyperextension, or more important still, forced lateral rotation of the chin or lateral inclination of the neck—commonly these three components are present together—seems often to increase the risk of paralysis, especially if they operate to increase the angle between the head and an abducted shoulder.* For this position the anaesthetist is usually responsible, often in his diligence to ensure an adequate airway and to leave a clear operation field. This is probably less true than it was in former years; so often now the airway is assured in almost any position of the head and neck by an endotracheal tube.

It is possible that the injury to the plexus is sustained not on the operating table itself but some time during the transport of the patient to and from the theatre, or even while in bed recovering from his anaesthetic. Injudicious manhandling from the table to the trolley and then to bed, when any considerable part of the body-weight is taken on the arms, may sometimes be responsible. An arm which is allowed to hang limp over the edge of the table, or to trail from the trolley and catch against an obstruction on the journey back to the ward is exposed to obvious dangers which must be diligently avoided.

OTHER AETIOLOGICAL FACTORS

A good deal of attention has been paid in recent years to the commonly occurring asymmetries of the thoracic outlet, which seem so often to render the neurovascular bundle at the root of the neck particularly vulnerable. Factors like the slope of the shoulder, the size and obliquity of the first rib, or the presence of a cervical one, however abortive, may predispose to the occurrence of post-operative paralyses; however, where such structural changes have been sought, as they have been diligently in a considerable number of the recorded cases, they have not been found. It is nevertheless true that deformities and disabilities of the arm or shoulder may seem sometimes to be in part responsible (*Brit. med. J.*, 1951).

Much more significant as an aetiological factor is the bulk of the patient. The bigger, heavier and stouter patient suffers most despite the generous buffering of the plexus which his collar of fat may offer, a happening which suggests that direct pressure on the main nerve bundle is an unlikely cause of the disability.

These paralyses have seldom been reported in children. This infrequency seems less to be related to the small bulk of a child than to the comparative rarity of long operations in children in the head-down position. Cases have recently occurred in paediatric practice following proctosigmoidectomy for Hirschsprung's disease.

* It is possible that occasional paralyses in the upper extremity following mastoid operations may be due to cervical disc displacement, the result of forcible manipulations of the head and neck under anaesthesia.

MECHANISM OF INJURY

The plexus or its main components may sustain injury from positioning of the p on the operating table in the following ways: (1) by compression; (2) by tr and (3) by a combination of (1) and (2).

Injuries by compression

Direct pressure.—The earliest contributors on the occurrence of this compl paid the closest attention to the effect of direct pressure on the plexus by sh rests, which, in the steep Trendelenburg position, support most of the body-w and a variety of yokes was designed to minimize liability to this particular t injury. The rests should, of course, be secured so that they lie directly opposi acromion processes, but if they are incorrectly applied at the outset, or if the pa position is moved, they may come to press deeply into the soft tissues betwe side of the neck and the point of the shoulder. It is, in fact, at least in the ca exceedingly difficult to bring any considerable pressure to bear on the plexus i way, deeply situated as it is low down in the posterior triangle and behind the cl However, this must be admitted as a possible way of sustaining damage to the p *especially when the patient is either spare or heavy and when the protective tone* trapezius and of the adjoining muscles has, during a long operation, been lost und influence of general anaesthesia supplemented often by curare. In any event, been maintained in the Courts that the use of ill-fitting or otherwise inade shoulder rests, imperfectly padded and wrongly adjusted, constitutes negligence.

"Nipping" of plexus between clavicle and first rib.—Büdinger, in first reportin occurrence of post-operative paralysis in the arm, attributed the injury to the ni of the plexus between the clavicle and the first rib, a mechanism which has in recent times been held responsible for both the nervous and the vascular mani tions of the "costo-clavicular syndrome" (Eden, 1939; Falconer and Weddell, and Falconer, 1947). This can readily happen only when the shoulder is both exte (retracted) and depressed. Under such circumstances nipping of the neurovas bundle may sometimes be demonstrable at operation. This is precisely the positi the shoulder when, in the Trendelenburg position and with the hands tucked u the buttocks, the shoulder girdle is strongly depressed by the checking table *The likelihood of serious compression of the plexus occurring in this way wou* increased (1) in the presence of some anomaly of the thoracic inlet, of which cer rib or a "post-fixed" plexus are among the most obvious; and (2) when the u muscle relaxants allows of a more complete descent of the shoulder girdle. Alth the risk of damage to the plexus in this way is hotly denied (*Telford and Mottersl* 1947), at least in a conscious patient and when there is no abnormality of the tho outlet, costo-clavicular nipping as a possible but, no doubt, infrequent cause of operative paralysis must be admitted.

Injury between clavicle and border of scalenus medius.—It is possible that whe shoulder is forcibly retracted the plexus may be caught between the clavicl scalenus anterior) and the sharp anterior border of scalenus medius, especially insertion runs forwards for some distance along the upper surface of the first This same mechanism may also operate during abduction of the arm.

Compression between clavicle and lower cervical transverse process.—There is to support the view that the plexus can be injured by compression between the cla and the lower cervical transverse processes.

Summary

On the whole there is little to justify the belief that compression of the plexus at point or another is a major source of injury at the time of operation. It is true

it has been shown (Denny-Brown and Brenner, 1944) that the primary cause of damage to a nerve submitted to a compression strain is the ischaemia which follows the obliteration of its vessels, but their experimental work also suggested that it is exceedingly difficult to cause such a disturbance in a really large nerve trunk.

Injuries by traction

A stretching force applied along its length would appear to be a much more likely cause of a plexus injury than would its simple compression. Both the rapidity and the quality of the functional recovery certainly suggest that the lesion in the great majority of the postural plexus injuries belong to the type which it is now the fashion to call neurapraxia (Cohen, 1942), a short-lived interruption of the functional capacity of the nerve without any significant structural change and certainly with no breach in the continuity of either the axis cylinders or of their supporting neurilemma sheaths. The main nerve trunks are relatively inelastic and somewhat vulnerable to any undue stretching strain, the motor fibres being much more susceptible to injury than are their companion sensory fibres (Sanders and Seddon, 1948). When the traction injury is more severe the axis cylinders may be disrupted and the epineural vessels damaged. This was shown convincingly by the experimental work of Denny-Brown and Doherty (1945). The immensely important neurilemma sheath is, however, preserved intact to support the regenerating axis cylinders (axonotmesis).

Pure stretching would be most likely to happen when some force was operating which tended to alter the position of the shoulder girdle in relation to the trunk, whether upwards, downwards, forwards, backwards, or in the direction of distraction. In the Trendelenburg position, for example, when the shoulder girdle is restrained on each side by a shoulder rest, the weight of the body tends to telescope the head and trunk downwards between the shoulders Securing the wrists to the table would have precisely the same effect, the patient being tethered to the table by the structures which join the shoulder girdle to the trunk, and among which are the main nerve bundles. In a curarized patient the burden on the plexus might well be an intolerable one. The greater part of the strain under these conditions would come to bear on C.5 and 6 (Stevens, 1934).

Injuries by combined traction and compression

The plexus is probably seldom subjected to a pure stretch along the line of the nerves, except perhaps in the rare event of an unconscious patient being manhandled by pulling on his arms.

Much more often the plexus is drawn tight over a fulcrum and subjected to a strain which is part stretching and in part compression The position of the fulcrum varies in different positions of the arm in relation to the trunk, and in general the part of the plexus which is most closely applied to the structure over which it is stretched or angulated would then seem likely to suffer most severely.

Forcible depression of the shoulder will stretch the plexus over the first rib or over the scalenus medius, and when the protective elevators of the shoulder girdle are completely flaccid, the strain on the nerve trunks might well be damaging.

In a proportion of healthy, conscious subjects extension and abduction—especially if this is to 90° or more—of the shoulder with the arm in full lateral rotation and the elbow straight, causes a discomfort which suggests that the plexus is then subjected to considerable tension This can be convincingly confirmed at operation as, for example, during the axillary dissection in radical mastectomy (Galley, 1950). In this position the head of the humerus is seen to project forwards covered by the subscapularis tendon, as a prominence over which the plexus is tightly stretched. This is all the more noticeable if, at the same time, upward movement of the shoulder

girdle and rotation of the scapula is restrained, for example, restraining shoulder rest (Fig. 50). The humeral head cannot the the way in a cranial direction, and the plexus becomes stretch

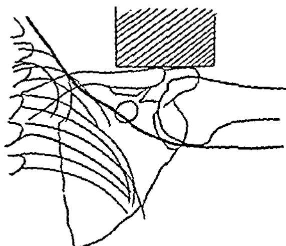


FIG. 50.—When rotatic vented by pressure the plexus becomes t prominent humeral (By cou

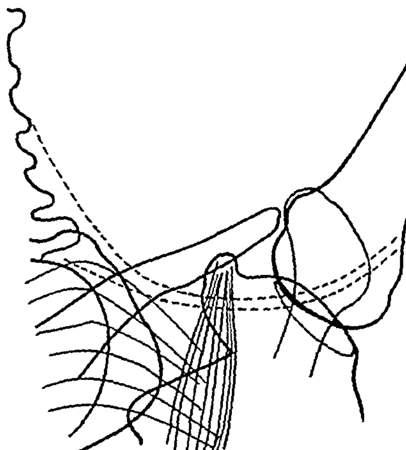


FIG. 51.—When the shoulder is in hyperabduction the pectoralis minor/cor is alleged to cause stretching and angulation of the plexus.

string (Cotton and Allen, 1903). Rotation of the chin and inclinat the opposite side makes matters worse. It is possible, too, that ir

stretching of the plexus over the humeral head at operation is the commonest cause of this type of injury.

In hyperabduction the mechanism is said to be slightly different. Wright (1945), and Beyer and Wright (1951) would have us believe that in this position the angulating agent is the sling or pulley formed by the insertion of pectoralis minor into the coracoid process (Fig. 51). This was not, however, the view of many of the earlier writers at a time when this type of plexus injury was commonly encountered (Cotton and Allen, 1903); and in more recent times Telford and Mottershead (1947) and Ewing (1952) have, at least in the cadaver, observed laxity of the plexus at this level even when the arm is strongly hyperabducted. Clausen (1942) believed that in this position the plexus may be pinched between the clavicle and the first rib. They do, in fact, then come rather close together, but as in the abducted and extended shoulder, stretching of the plexus over the prominent humeral head is likely to be the most important cause of injury.

Assessment of the relative parts played by the various structures which adjoin the plexus in the root of the neck and in the axilla, and which act either as compressing agents or as fulcra over which the plexus is stretched, is for the most part speculative. Such autopsy findings as are available have not revealed the presence of any gross or microscopic changes in the nerve trunks (Budinger, 1894). It is apparent that the possible mechanisms of injury are many, and as accumulating experience of the somewhat allied problem of the costo-clavicular syndrome suggests, the subject is probably much less simple than we often suspect Certainly it is quite impossible to forecast with any degree of certainty the type of paralysis which is likely to be sustained by the plexus with the arm in any one position. Experience also suggests that the vulnerability of the plexus varies widely from one patient to the next and that paralysis happily does not follow every ill-chosen positioning of the arm at operation.

PREVENTION

Although admittedly time-consuming and an irksome source of delay, it is essential in the avoidance of plexus injury that the positioning of the patient at the beginning of the operation should be supervised with consummate care. This is especially the case when embarking on what is likely to be a long operation, and the more so if the patient is big or overweight Every effort should be made in so adjusting the patient as to anticipate every likely contingency, and to avoid the hurried fumblings and alterations under the towels later in the operation, which are so often the prelude to postural nerve injuries.

Although in law either the surgeon or the anaesthetist may be held responsible (*see* page 58), it would seem reasonable that at this point in the operation the surgeon should proceed only when he is completely satisfied that the positioning of the patient is to his liking.

It is not enough to check the positioning at the start of the operation. One is obliged to watch it carefully throughout the duration of anaesthesia. Insidious but considerable changes may occur in the relative positions of the arm and the trunk during the course of a long operation, be it from the patient gradually slipping down a tilted table or from changes in the degree of abduction of the arm, often from the pressure of assistants or of the surgeon himself. The unthinking anaesthetist may be also careless in this respect.

Quite the most dangerous position of the arm is that of abduction. It must never be brought out from the side beyond an angle of 90°; 60° or less is much safer. It is probably wise to insist that the arm should under no circumstances be abducted (1) when the patient is in the Trendelenburg position with shoulder rests fitted; and (2) when some form of support has been introduced to arch the dorsal spine, as in an operation on the biliary tract.

The only position of real safety for the arms is lying adequately padded down by the side of the body with the minimum of restraint and protected from noxious pressure either from the table or from the surgeon or both. Browne and Roberts (1950) have described a very simple Perspex splint which serves admirably to safeguard both the arm and the infusion needle (Fig. 52). The malleable lead arm used by Howkins (1952) was designed for the same purpose. Care must be taken that in the head-down position none of the restraining force to the pull of gravity is then taken by the arms. A simple and safe way of disposing of the arms is by crossing them over the chest and tucking them away under the operation shirt. This has the disadvantage of being a somewhat clumsy manoeuvre and the arms tend to be very much in the way if we wish to explore the upper abdomen. Alternatively, the arm can be brought across the chest and the elbow secured to the opposite shoulder rest by adhesive strapping; the hand now comes to lie on the patient's face and here the veins on the dorsum are readily accessible for puncture (Clutton-Brock, 1949). The veins on the back of the

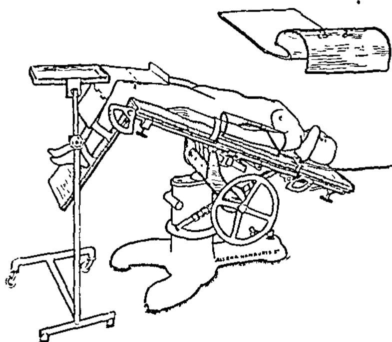


FIG. 52.—Perspex arm shield designed by Browne and Roberts (1950) to protect the "infusion arm" while in the adducted position (By courtesy of "The Lancet,".)

hand and wrist are also accessible when the arm is folded on the thorax and the hand secured with strapping to the skin of the chest wall (Howkins, 1952).

A device which seeks to achieve the same position but rather more effectively and certainly more neatly has been described by Sinclair (1950). A vertical metal rod with a right-angled bend directed across the front of the chest is erected in the shoulder region. For abdominal operations each arm is hung from such a sling; for radical mastectomy or any similar procedure only the arm on the affected side need be so secured.

Kiloh (1950), who reported four cases of plexus paralysis following cholecystectomy, advocates the use of a gall-bladder harness which consists of two adjustable leather cuffs, joined by a piece of padded chain which passes behind the patient's neck. The arms are adducted and the elbows flexed, the supinated hands lying in front of the shoulders. However undesirable the abducted position of the arm may be, it must be freely admitted that this is often the only expedient way of disposing of it. When the patient is supine and horizontal, and the arm is brought out to something less than a right angle, with the elbow flexed, the hand pronated and the shoulder in a comfortable degree of internal rotation, the hazard to the plexus is not great. This is quite the most convenient position for the anaesthetist and it is also that which most

readily gives emergency access to a good vein during the course of an operation. Provided all concerned are fully aware of the risks involved in any abducted position of the arm, little harm is likely to result. If an arm is brought out from the side to give access to a vein or to the operation field, it should never be secured back to an arm-board tucked under the mattress. Every effort must be made to avoid extension at the shoulder by padding the arm support generously in order to build it up and bring the arm to lie anterior to the mid-coronal plane of the trunk. Whenever possible veins should be used on the dorsum of the forearm, wrist or hand so that the hand can be pronated and the elbow left in flexion. It is true that the arm in only a mild degree of abduction is likely to get in the surgeon's way, but this is a nuisance which must be accepted with reasonable tolerance. Calls to increase the angle of abduction must be strenuously resisted.

Whenever the operation is likely to be a long one it is wise to choose a vein at the ankle for venoclysis, if the position of the leg and the site of the operation allow. If fear of a troublesome and indolent thrombosis at this site—or the all too frequent painful, infected, slowly healing incision—is thought to be a compelling reason for

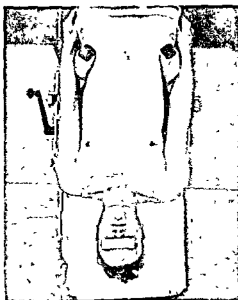


FIG. 53—Patient in steep Trendelenburg position with arms comfortably adducted and body-weight taken by padded iliac-crest supports of the Ogier Ward pattern.

the use of an arm vein, it is wise to expose a good vein in the forearm, and to insert a polythene tube leaving the arm adducted to the patient's side and removing the infusion stand to a convenient distance. Gray (1950) has suggested the more frequent use of the external jugular vein which he believes can be cannulated percutaneously with no great difficulty.

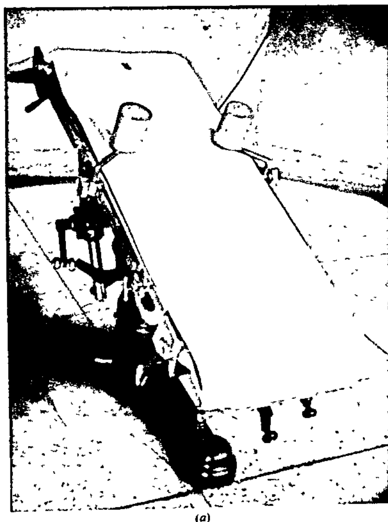
Under no circumstances should both arms be abducted simultaneously: this is a manoeuvre which invites the risk of a bilateral lesion. Worse still is fixation of both arms in abduction to a double arm-board. Hyperabduction of the shoulder is dangerous whatever may be the position of the trunk.

The wrists must never be secured to the top of the table. When the arm must, for some very good reason, be drawn up beside the head it would seem wise to pull only on the scapula—as is commonly the practice in thoracic operations, and then only after it has been freely mobilized by division of the muscles which secure it to the thoracic cage—and to take good care that the arm follows it closely.

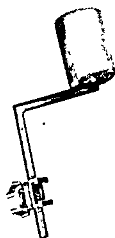
The head should always be kept in the neutral position, this is all the more important when the arm is abducted on one side. Extension of the head, lateral rotation of

the chin or lateral deviation of the neck—these latter two to the side opposite to the abducted arm—all increase the strain on the plexus.

Of all the positions in which the closest lookout must be maintained at all times to prevent plexus injury, those in which the patient is lying in the head-down position are the most important; commonest among them are the Trendelenburg position and its modification, as, for example, when completing a synchronous combined abdomino-perineal resection with the aid of the Lloyd-Davies (1939) leg supports. Every device must be employed to prevent any of the weight of the body being taken by the arms or shoulder girdle. Securing the legs with the knees flexed over the dropped leaf of the table gives some security, but only at the expense of undesirable



(*a*)



(*b*)

FIG. 54.—(*a*) Wood-Smith supports fitted to a standard operating table. (*b*) Wood-Smith's (1953) modification of one Ogier Ward pelvic support. Its height can be adjusted to accommodate patients of different build and the rotating padded cylinder fits snugly against the iliac crest. (*By kind permission of Dr. Wood-Smith.*)

and sustained pressure on the calf veins with the possible sequel of phlebo-thrombosis. Experience suggests that the only really safe way of supporting the trunk is by the use of rubber-covered iliac crest supports as used by Ogier Ward (1950) at St. Peter's Hospital, London (Fig. 53). These are designed in two sizes, one for the big and stout and the other for the thin and spare. They are made to fit snugly into the soft tissues between the rib margin and the ilium. Experience proves that they can, even in the conscious patient, confidently and comfortably sustain the body-weight even when in the steepest head-down position. Since there is no question of weight transference from the shoulder to the trunk, there is no hazard to the plexus, at least from this cause. It is true that the left support may be somewhat in the way when an incision must be made close to the left iliac spine, as when fashioning an iliac colostomy, but the operation can usually be so planned that this step is left until the resumption of the horizontal

Those who scorn to use pelvic supports will inevitably be confronted by plexus paralyses sooner or later. It is never safe to rely on the traditional shoulder rests, for however adequately padded and carefully positioned so as to take pressure opposite the acromion process, they suffer from the fundamental fault of retaining the weight of the body only through the agency of the structures which secure the arm to the trunk, and among them must be included the brachial plexus.

It will, of course, from time to time in any varied surgical practice prove necessary for the proper conduct of an operation to place the arm in a position which experience has shown introduces the risk of plexus injury, it is obvious that the greatest care should then be taken to reduce the time the patient is in this position to the absolute minimum. If should, for example, be an invariable practice to employ the Trendelenburg tilt for not one minute longer than is necessary; the horizontal position is a good deal safer.

In general, every effort should be made to reduce the period of anaesthesia to the absolute minimum, especially when the procedure is likely to be a long one. It is as important to save time in the preliminaries as in the actual operation itself. This is particularly true when curare is being used, with the patient with a head-down inclination; it is equally true of any operation in any position.

The use of intravenous muscle relaxants should be restricted as far as possible to those phases of the operation when they are absolutely necessary, and whenever they are employed extreme vigilance must be exercised in every manipulation and positioning of the patient.

Orderlies, porters, nurses, dressers and all those who play any part in the handling of the unconscious patient must be made acutely aware of the vulnerability of the plexus and of the necessity to practise the greatest care during every manipulation. Under no circumstances should any of the body-weight be taken on the arms when lifting an unconscious patient: to let an arm drop down by the side of the table, or to allow it to trail from the side of a trolley and catch on some obstruction is a careless act which may be fraught with disastrous consequences

It must be admitted that these post-operative plexus injuries are not in every instance avoidable. Even when every member of an operating team is alerted to their prevention, they will still occur. It is a risk, although fortunately a remote one, which must accompany every operation under general anaesthesia. It is equally true that both their frequency and their severity can be very substantially reduced by unremitting attention to the position of the patient's arms during every phase of the anaesthesia, including induction and recovery Wood-Smith (1952b) has very neatly expressed the risk of paralysis by the formula plexus injury = degree of inhibition of muscle tone × time × strain on plexus. In the prevention of post-operative paralysis we must continuously strive to reduce to the absolute minimum the value of each of these factors

TREATMENT

In the great majority of cases recovery is both spontaneous and rapid. In the more complete lesions—and this is especially so in the bilateral case—every effort must be made to mitigate the mental distress of the disability, by patient nursing and by anticipation of the patient's every need.

Treatment is confined to judicious splinting of any paralysed muscle groups and by assisted active and gentle passive movements until recovery is complete. Any cumbersome appliance is best avoided; simple support of the limb on pillows is

usually enough. In the few more serious types of injury, galvanism may be of some value in preventing a severe degree of muscle wasting.

PROGNOSIS

Fortunately, in general, both the speed and the quality of the functional recovery are favourable. Sensory recovery is especially dramatic. Subjective sensory disturbances have usually disappeared after a few days, and a complete return of all sensory function is generally recorded in the early weeks. Significant residual sensory loss is unusual; permanent and complete anaesthesia in even a small patch of skin is virtually unknown.

Spontaneous and rapid return of motor function is also the rule, the paralysis in the least seriously affected muscles disappearing first. Even when there is, at the outset, complete loss of power in the entire upper extremity, the patient has usually regained some movements in the hand by the time the operation wound is healed. In the milder cases (neurapraxia) the paralysis may clear up entirely in 6–7 weeks, and even when the injury is severe and widespread (axonotmesis) recovery is usually complete in 6–9 months. Although in many of the recorded cases there has still been at this stage some residual muscle weakness—most often of the biceps and of brachialis—there have been few reports of a longer follow-up. Unhappily, permanent motor paralysis may result, although rarely, and be the cause of a considerable disability to the labourer who misses his elbow flexors or the skilled worker who loses fine movements in the hand. These are the cases which tend to feature in litigation, and the disability in such cases is, of course, often exaggerated by functional overlay, a feature which ceases to operate as soon as the terms of a final settlement are agreed upon.

MEDICO-LEGAL ASPECTS

Although claims for injury sustained to the brachial plexus during the course of surgical operations have come to litigation from time to time since the beginning of the century—Hersman, writing in 1901 was certainly conscious of this risk—the number of cases considered in the Courts has increased significantly within recent years. This may reflect in part the increasing frequency with which patients seek redress on charges of negligence, but it seems likely that there has been a real increase in the incidence of this complication.

The plaintiff has sued sometimes the surgeon and sometimes the anaesthetist, sometimes both of them, or alternatively the hospital. The responsibility of the surgeon and of the anaesthetist has in this respect never been clearly established, with the not unnatural result that neither may feel primarily concerned and reasonable precautions may, in consequence, go by default. It would seem wise for every surgeon and his anaesthetist to come to some agreement in this respect, and to take steps to make every other member of the team keenly aware of this operation hazard. However desirable it is that one man, and he most properly the surgeon, should, like the captain of a ship, accept ultimate responsibility, it is obviously impossible for him at every phase of the operation to maintain constant supervision of the position of the arm. It would seem wise for both the surgeon and the anaesthetist to give their assent to the positioning of the patient before the operation is actually begun. Thereafter each must answer for the consequences of any change made under his direction. It has become so uniformly the practice these days for the anaesthetist to use the arm for injection or for the application of a sphygmomanometer cuff, and he has now so clearly won his place in the eyes of the law as a specialist with his established rôle in the conduct of any operation, that it would seem reasonable to expect him to assume, in the main, the responsibility for safeguarding the plexus, certainly from the moment when the surgeon has made his skin incision. When, however, at the instance of the

surgeon, he is obliged to alter the position of the arm, the responsibility is clearly the surgeon's. This would especially be the case if the arm is put in a position which however necessary for the conduct of the operation, is still undesirable because of some especial hazard to the plexus.

In the main it has been held that such lesions are largely preventable and that there has been negligence when there has been a clear omission to correct all the faults in a position on the table which experience has shown to predispose to injury. An anaesthetist was, for example, held culpable for giving an intravenous anaesthetic when the arm was strapped above the patient's head (*Brit. med. J.*, 1951), and more recently an anaesthetist was considered negligent in not avoiding abduction of the arm to too great a degree and for longer than was necessary (*The Times*, 1953).

(*See also British Surgical Practice* Brachial Plexus, Vol. 2, page 315, S. Key 70.)

REFERENCES

Beyer, J. A., and Wright, I. S (1951) *Circulation*, **4**, 161.
British Medical Journal (1951). **1**, 1147.
Browne, J. C. M , and Roberts, H (1950). *Lancet*, **1**, 278.
Büdinger (1894) *Arch. klin. Chir.*, **47**, 121
Cohen, H. Quoted by Seddon, H J. (1942) *Brit. med. J.*, **2**, 237.
Cotton, F. J., and Allen, S W (1903). *Boston med surg. J*, **148**, 499.
Clausen, E. G. (1942). *Surgery*, **12**, 933.
Clutton-Brock, J (1949) *Anaesthesia*, **4**, 141.
Denny-Brown, D., and Brenner, C. (1944) *Arch. Neurol Psychiat.*, **51**, 1.
— and Doherty, M. M. (1945). *Ibid.*, **54**, 116
Eden, K. C. (1939) *Brit J. Surg.*, **27**, 111.
Ewing, M. R. (1950). *Lancet*, **1**, 99.
— (1952). Unpublished data.
Falconer, M. A. (1947). *Brit. med. J*, **2**, 69.
— and Weddell, G (1943) *Lancet*, **2**, 539
Galley, A. H. (1950) *Lancet*, **1**, 184.
Garrigues, H. J (1897) *Amer. J. med. Sci.*, **113**, 81.
Gray, A. J. (1950). *Lancet*, **1**, 184.
Hans, S F. (1952) *Lancet*, **2**, 664
Hersman, C. C. (1901) *J Amer. med. Ass* , **36**, 231
Howkins, J. (1952). *Lancet*, **2**, 759
Kiloh, L. G (1950). *Lancet*, **1**, 103.
Lloyd-Davies, O. V. (1939) *Lancet*, **2**, 74.
Pommerenke, W. T , and Risteen, W A (1944) *Amer J. Obstet. Gynec* , **47**, 395.
Raffan, A. W. (1950) *Brit med. J.* **2**, 149.
Sanders, F K., and Seddon, H. J. (1948) *British Surgical Practice*, Vol 2 London; Butterworth.
Sellors, T. H. (1950) In *Techniques in British Surgery*, p 179 London; Saunders.
Sinclair, A. D (1950). *Lancet*, **1**, 592
Sinclair, R. N. (1948) *Glasgow med J* , **29**, 378.
Slocum, H. C., O'Neal, K C , and Allen, C R (1948) *Surg. Gynec Obstet.*, **86**, 729.
Stevens, J (1934) In *The Shoulder*, by S A Codman. Boston, Saunders.
Sweet, R. H (1950). *Thoracic Surgery* Philadelphia, Saunders.
Telford, E. D., and Mottershead, S (1947) *Brit med J* , **1**, 325
The Times (1953). 23rd April.
Turney, H. G (1899) *Clin J* , **14**, 185.
Ward, R. O. (1950) *Lancet*, **1**, 423.
Wood, D. A. (1940) *Calif. West. Med* , **53**, 267
Wood-Smith, F. G (1952a). *Brit. med. J* , **1**, 1115.
— (1952b) Personal communication
— (1953) In the Press
Wright, I. S. (1945). *Amer. Heart J.*, **29**, 1.

THE SYNDROME OF THE CAROTID SINUS

By Sir JAMES LEARMONTH, K.C.V.O., C.B.E., Ch.M., F.R.C.S.E.
Regius Professor of Clinical Surgery and Professor of Surgery, University of Edinburgh

and

RICHARD TURNER, O.B.E., M.D., F.R.C.P., F.R.C.P.E.
Senior Lecturer in Medicine, University of Edinburgh;
Physician, Western General Hospital, Edinburgh

INTRODUCTION

The increased interest shown by clinicians in the syndrome associated with hypersensitivity of the carotid sinus reflex is reflected in the large number of papers which have been published on this subject in recent years. Nevertheless, there is still need for more widespread recognition that hypersensitivity of the carotid sinus may be one of a number of causes producing certain clinical features to be described in this paper. The term "carotid sinus syndrome" is applicable only when these clinical manifestations can be constantly reproduced by pressure over one carotid sinus, or over each.

ANATOMY

Position

The term "carotid sinus" is applied to the slight dilatation of the carotid arterial system which usually includes the termination of the common carotid artery and the beginning of the internal carotid artery, although it may be limited to the latter. The line of the common and external carotids is from the corresponding sternoclavicular joint to the interval between the angle of the mandible and the mastoid process; usually the bifurcation of the common carotid corresponds to a point on this line at the level of the superior border of the thyroid cartilage. The bifurcation may be higher (above the hyoid bone, 1 in 30 cases; opposite the hyoid bone, 1 in 5 cases) or lower (opposite the cricoid cartilage, 1 in 60 cases, opposite the middle of the thyroid cartilage, 1 in 12 cases). The wall of the carotid sinus is unusually rich in elastic fibres.

Nerve supply

In relation to the fibrous tissue of the adventitia of the carotid sinus there are sensory end-organs (baroreceptors) whose axones are collected on the antero-lateral surface of the internal carotid artery into a fine filament which is joined by fine nerves from the carotid body; the composite nerve forms the ramus caroticus of the glossopharyngeal nerve. This ramus inclines posteriorly as it ascends to join the parent nerve where the latter is approaching the internal carotid artery; less commonly the ramus caroticus joins the pharyngeal branches to the glossopharyngeal nerve, or its branch to stylopharyngeus. During its course the ramus caroticus communicates with branches of the vagus nerve (50 per cent of cases) and with branches of the superior cervical sympathetic ganglion.

PHYSIOLOGY

General

For 150 years it has been known that pressure on the neck of a patient applied in the line of a common carotid artery may result in slowing of the heart. It was assumed that the bradycardia was a result of stimulation of the underlying vagus nerve until it was shown that although the response was mediated through the vagi, it was primarily dependent on a reflex originating in the carotid arteries, and that pressure upon a carotid sinus might produce a fall in blood pressure in addition to bradycardia (Galdston, Goldstein and Steele, 1943)

Hering (1927) made detailed anatomical and physiological studies of the reflex in animals, and his work has been confirmed and extended by Heymans and his co-workers (1933). The present conception is that the stimulus which initiates the carotid sinus reflex is not the pressure within the sinus, but the state of contraction of its walls, which depends upon their resistance to stretching (Heymans and van den Heuvel-Heymans, 1950). When the pressure within the sinus is increased, its walls normally stretch, and bradycardia and a fall in blood pressure occur (depressor response); if, however, the walls of the sinus are mechanically prevented from stretching, increased intra-carotid pressure does not trigger the reflex. When the pressure is decreased, the walls normally contract, and cardiac acceleration and rise in blood pressure occur. The general physiological importance of the reflex lies in the mechanism it provides for ensuring that the arterial blood supply to the brain shall be kept as constant as possible, despite abrupt changes in the relationship of the head to the remainder of the body, as, for example, by a change from the lying to the erect position.

Hominal

In man the sensitivity of the carotid sinus to pressure applied over it varies widely in normal individuals. In a group of nearly 2000 persons, Sigler (1943) found that in about two-thirds of those aged under 20 years, the depressor response could not be elicited; of those aged over 60 years, about two-thirds showed a depressor response to pressure. "Normal" responses are small; they do not exceed a slowing of 5 beats per minute, and a fall in blood pressure of 10 millimetres of mercury. The technique of attempting to elicit the depressor response will be described later (page 64). When cardiovascular disease is already present, the depressor reflex can be more easily obtained. On examining 700 such patients Sigler (1942a) found that a fall of pressure of more than 10 millimetres of mercury occurred in 78 per cent of males and 71 per cent of females The response occurred more often and to a greater degree in the older age-groups; and the higher the original blood pressure the more frequent was the response and the greater its degree. A fall in systolic pressure was more common than a fall in diastolic The amount of stimulation required to produce the maximum response varied from patient to patient, and in many cases there was a distinct difference between the responses of the two sides. Sigler concluded that in persons who show a marked vasodepression induced by the carotid sinus reflex there was inherent instability of the vasomotor system, either in the medullary synapses or in the vasomotor terminals in the arterial tree.

PATHOLOGICAL PHYSIOLOGY

The possibility of applying the work of Hering and of Heymans to explain certain pathological states in man was first emphasized by Weiss and Baker (1933) who demonstrated that hypersensitivity of the carotid sinus mechanism can initiate unconsciousness, convulsions and various relatively minor autonomic disturbances.

Unconsciousness and convulsions are usually the result of cerebral anoxaemia, either from cardiac asystole or from primary reflex depression of the blood pressure, but occasionally unconsciousness occurs in the absence of changes in either heart rate or blood pressure.

The afferent and efferent portions of the reflex arcs concerned lie within the autonomic nervous system; although the afferent pathway is always the same, the sinus nerve and the efferent pathways vary, the vagus being the pathway to the heart and the sympathetic to the blood vessels.

Types of response

Weiss and Baker described three main types of the carotid sinus syndrome, and these have been accepted by most subsequent writers. The occurrence of any one particular type depends upon the dominant efferent response to stimulation of the sensitive carotid sinus.

Vagal type.—This is characterized by severe bradycardia, and cardiac asystole from sino-auricular or atrioventricular block which results in acute cerebral anoxaemia. The attack can be ended by the intravenous injection of atropine (which paralyses the vagus) or prevented by previous subcutaneous injection of adrenaline (which stimulates the ventricles).

Depressor type.—Least common is the depressor type and it is usually associated with one of the others. Efferent impulses to the arterial tree cause generalized vasodilatation and depression of blood pressure, which is not related to slowing of the heart rate; if the fall in blood pressure is extreme, cerebral anoxaemia results. Atropine does not end the attack, but the injection of adrenaline will do so.

Cerebral type.—During the attack there is no change in the heart rate or in blood pressure, and the blood flow through the brain is normal. Impulses from the carotid sinus to the medulla are relayed to the vegetative centres in the hypothalamus, and sudden loss of consciousness results. Both atropine and adrenaline are without effect.

Mixed types—Various combinations of the above types may occur.

Galdston and his colleagues (1943) examined these various responses in man by utilizing modern methods of recording direct intra-arterial pressures and pulse rates. They found that the most common circulatory response was slowing of the heart and asystole (vagal response) together with a fall in arterial pressure (depressor response). A pure vagal response was the next most common, but a pure depressor response was not observed except when the patient was under the influence of atropine. They confirmed the separate occurrence of the cerebral type.

CLINICAL FEATURES

General

Hypersensitivity of the carotid sinus reflex giving rise to spontaneous symptoms is uncommon, though not rare. As in many other relatively obscure conditions, the correct diagnosi [illegible]
carotid sinus is [illegible]
gations are mad [illegible]
cardiovascular [illegible]
obvious cause can be found on clinical examination. The attacks occur at varying intervals, may happen without any warning or may be preceded by such warning sensations as giddiness, weakness and epigastric distress. Between the major attacks of syncope there may occur various minor manifestations similar to the premonitory symptoms. Unconsciousness usually lasts for a minute or two and after-effects are uncommon; the patient usually feels quite well immediately he recovers consciousness.

Age and sex

All authors are agreed that the syndrome is commoner in the older age-groups and in males. Thus Nathanson (1946) found that 70 per cent of his patients were aged 50–70 years and that 85 per cent were males.

Predisposing factors

Recorded predisposing factors include fatigue, emotion, menstruation and the pharmacological action of digitalis. Emotional instability and neuroses of various types and varying severity are common in those subject to carotid sinus syncope, but they appear to be part of the constitutional make-up of the individual rather than the result of the attacks; emotional upsets may precipitate attacks.

Precipitating factors

General

There is general agreement that in most attacks precipitating factors are absent. Draper (1950) reviewed the reports of cases published in 16 papers and found that precipitating factors were mentioned in only 30 per cent of these. Precipitating factors include sudden movements of the head and neck, the pressure of a tight collar, changing from the supine to the erect posture, coughing, shaving, carrying heavy loads on the shoulders, blows on the neck, resting the head on the hand and straining during defaecation.

Local

Local abnormalities in the form of tumours or enlarged cervical glands may press upon the carotid sheath, but such pressure only rarely evokes the reflex. McSwain and Spencer (1947) found reports of six cases due to the presence of a tumour of the carotid body, and added two similar cases Ferris, Capps and Weiss (1937) considered that arteriosclerotic changes in the wall of the carotid artery facilitated the transmission of external pressure to the receptors in its wall. On the other hand, Sigler (1942a) pointed out that the greater effect of pressure when the patient is upright did not support the hypothesis that a local abnormality played a part. Moreover, many patients with sclerotic carotid arteries do not have hypersensitive carotid sinuses.

Associated cardiovascular disease

A scrutiny by Draper (1950) of 59 cases reported in the literature disclosed evidence of arteriosclerotic or hypertensive cardiovascular disease in 48 of these (81·4 per cent). A number of authors have stressed the frequency of associated coronary disease. In some cases pain indistinguishable from that of angina pectoris has been a feature of the syndrome. This could be reproduced by pressure over the hyperactive carotid sinus, although no objective evidence of coronary disease could be found. Sigler (1942a) thought that the syndrome rarely occurs in the absence of coronary disease; he considered hyperactivity of the carotid sinus mechanism to be useful evidence for the diagnosis of coronary disease. Similar symptoms were produced by angina of effort, myocardial infarction and pressure over the carotid sinuses. The evidence suggests that coronary blood flow can be affected by stimulation of the carotid sinus reflex.

Abdominal manifestations

Stern (1938) studied a patient who had attacks of lower abdominal cramps ending in defaecation, preceding giddiness which was followed by syncope. The attacks could be reproduced by pressure over the carotid sinus, and were accompanied by a

fall of blood pressure and bradycardia. A sensation of fullness in the head, numbness of the hands and sweating were other features of induced attacks and it was concluded that these various manifestations were due to widespread autonomic discharge. Similar manifestations were noted by Tanney and Lilienfeld (1942).

Engel and Engel (1942) found hypersensitivity of the carotid sinus to be present in 18 of 23 patients with acute disease of the biliary tract, and concluded that summation of afferent impulses from end-organs in the biliary tract had occurred, which reached the threshold of reaction of vagal centres in the medulla. Sigler (1942b) criticized this conclusion, and considered that coronary disease could explain the hyperactive reflex in the cases mentioned, and that the angina was probably due to coronary insufficiency possibly secondary to reflex vasospasm initiated by impulses from the abdominal organs.

Reproduction of attack

Hypersensitivity of the carotid sinus reflex should be considered in every patient in whom the causation of episodes of syncope, convulsions, vertigo, giddiness, light-headedness or paraesthesia is obscure, and an attempt should be made to reproduce an attack by pressure on each sinus in turn. The patient should be sitting upright, because in this position an attack is more likely to be evoked than when he is lying down, and the face should be turned slightly to the opposite side. Over the usual position of the carotid sinus steady pressure should be exerted by the tip of the index finger, posteriorly and a little medially, for 10–15 seconds.

Dangers

It is important to realize that in middle-aged or elderly arteriosclerotic individuals attempts to elicit the reflex are not without danger. Weiss and his colleagues (1936) showed that the cerebral ischaemia which may follow pressure upon the sinus is not due to mechanical occlusion of the common carotid artery; they assumed that reflex vasoconstriction of the branches of the internal carotid artery occurred on the same side, and advised that only one side should be tested at a time because of the danger of evoking the reflex from both sides by simultaneous bilateral compression. Askey (1946) reported on 10 untoward incidents following compression of the sinus. In seven cases hemiplegia was the direct result of stimulation of the sinus, and in another it occurred 24 hours later; the hemiplegia was always on the opposite side of the body. In two patients symptoms of temporary cerebral irritation were produced. Marmor and Sapirstein (1941) recorded the case of a patient who collapsed and died a few minutes after the reflex had been elicited; post-mortem examination showed bilateral thrombosis of the anterior cerebral arteries, and a moderate degree of atheroma of the other cerebral arteries, and they point out that stimulation of the sinus should not be unduly prolonged—if continued after syncope has occurred death may ensue. Nathanson (1946) stated that massage of the sinus should be avoided.

Subjective manifestations

Giddiness, faintness and blurring of vision usually precede syncope, but they may occur as the only manifestations of hypersensitivity. Other complaints include weakness, ringing in the ears, confusion, paraesthesiae and an unpleasant sensation of epigastric distress.

Objective manifestations

Pallor and sweating may precede loss of consciousness. If the pressure is maintained, twitching or convulsions may develop. Sometimes convulsions may occur without any significant changes in the dynamics of the circulation. Circulatory changes include a fall in blood pressure, slowing of the heart, and asystole. Hyperpnoea

commonly occurs and is independent of the circulatory response. Galdston, Goldstein and Steele (1943) showed that hyperpnoea is not prevented by anaesthesia produced by barbiturates, but that it is abolished by local infiltration of the region of the sinus with procaine; they concluded that hyperpnoea is due to disturbance of the blood supply of the carotid body and not to mechanical stimulation of the carotid sinus.

Electrocardiographic records

In many (perhaps most) patients electrocardiograms made before an attack is induced show evidence of pre-existing cardiac disease. When the hypersensitive sinus is stimulated, records may show in addition complete heart block, suspension of ventricular contractions with continuance of auricular contractions, and ventricular extrasystole. These additional features of the electrocardiographic record are not of diagnostic importance.

Electro-encephalographic records

Using routine electro-encephalographic methods, Forster, Roseman and Gibbs (1942) found no gross disorder of cortical rhythm during the syncope of the carotid sinus syndrome. However, spectrum analysis with the Grass analyser showed a slowing of cortical activity during the period of unconsciousness in the majority of cases exhibiting the circulatory type of carotid sinus hypersensitivity.

In seven cases of the cardio-inhibitory type, Engel, Romano and McLin (1944) demonstrated slow waves of moderately high voltage, but similar waves were present in syncope from other causes and appeared to be related to the duration of unconsciousness; in the syncope of the carotid sinus syndrome no specific type of electro-encephalographic response could be demonstrated

Evaluation of tests

We emphasize that the reproduction of a typical attack by stimulation of a carotid sinus is the only evidence upon which the diagnosis of "carotid sinus syndrome" can be made. Only one sinus may be hypersensitive; if the condition is bilateral, usually the attack is much more easily elicited by pressure on one side than on the other.

MEDICAL TREATMENT

Patients who have symptoms referable to a hypersensitive carotid sinus are often nervous individuals, and naturally attacks of syncope are alarming. It is important to explain the nature of the attacks to such a patient, and to reassure him that they are not due to any disease of the heart, brain or other vital structure.

Preventive measures

Preventive measures should include advice to avoid (1) sudden movements of the head and neck such as turning the head quickly and looking up or stooping suddenly, (2) constriction of the neck from the wearing of a tight collar, and (3) any factor such as forceful straining or coughing which may have precipitated previous attacks.

Sedation

Sedative drugs (phenobarbitone or one of the other barbiturate or allied drugs) tend to reduce the incidence of attacks.

In the treatment of associated cardiac disease, digitalis should, if possible, be avoided owing to its reputed action in sensitizing the carotid sinus reflex arcs.

In the treatment of any associated condition, drugs (for example, Mecholyl) which stimulate the parasympathetic system should be avoided.

If the attacks are of the vagal type, $\frac{1}{120}$ grain of atropine sulphate three times daily

may be given; if atropine is not tolerated, a trial may be made of ½ grain of ephedrin sulphate three times daily, with or without phenobarbitone.

If the attacks are of the depressor type, ½ grain of ephedrine sulphate three time daily may be tried.

Drugs, other than general sedatives, are not of any value in the cerebral type.

SURGICAL TREATMENT

Indications

Surgical treatment may be considered in the vagal and depressor types of attack whe medical treatment fails to control the number or the severity of attacks, or both, o when atropine cannot be tolerated and ephedrine is inadvisable—for example, in hypertension. It is the only form of treatment likely to relieve attacks of the cerebral type. Occasionally the patient's occupation necessitates his regularly making the movement which precipitates an attack; in such cases operation should be advised as the primary treatment.

The patient should not be under the influence of digitalis; and in the pre-operative medication morphine is best avoided, since there is some evidence that it sensitizes the carotid sinus (Rovenstine and Cullen, 1939).

Anaesthesia

Some form of inhalation anaesthesia is to be preferred and we have found cyclopropane suitable. During the induction of anaesthesia the patient must be kept with the face looking upwards, and care must be taken to avoid pressure from the mask or from the hands of the anaesthetist upon the region of the sensitive sinus until unconsciousness is produced. It is known that the establishment of deep general anaesthesia abolishes the reflexes originating in the wall of the carotid sinus, but until the patient is unconscious the risk of precipitating an attack must be carefully avoided.

Position of patient

When anaesthesia has been produced, the patient's head should be turned to the side opposite to that of operation, and the neck should be supported by a narrow firm sandbag.

Technique

An incision is made along the anterior border of the sternomastoid muscle, from the level of the angle of the jaw to the level of the isthmus of the thyroid gland (Fig 55). It is deepened through the platysma and the deep cervical fascia to expose the carotid arterial system, crossed at intervals by tributaries of the internal jugular vein; it may be necessary to retract the omohyoid muscle medially (Fig. 56). The tributaries of the internal jugular vein are divided between ligatures and the vein is then freed from the artery for a distance of 4 centimetres below and 4 centimetres above the carotid bifurcation (Fig. 57). The descending branch of the hypoglossal nerve is identified and held out of the field of the operation by a moist tape. The common, internal and external carotids are then freed from their bed in the carotid sheath for a distance of 4 centimetres proximally and distally from the bifurcation; they may be controlled by tapes, or in the first instance held forward by a moist swab placed beneath them. The adventitia is raised from the media of the common carotid and its two branches by injecting beneath it, *through a fine needle, a sufficient amount of* weak procaine solution (0·5 per cent); the injection is begun in the region of the sinus (Fig. 58). An incision is then made in the adventitia over the proximal part of the common carotid artery and it is stripped from the artery by sharp dissection, first on one side and then on the other, the vessel being rotated by tapes to facilitate this part of the dissection

(Fig. 60). Difficulty may be encountered when the region of the bifurcation is approached posteriorly because of a low origin of the ascending pharyngeal artery (Fig. 59), and care must be taken at this point that this artery is not torn at its origin from the parent vessel. It may be that, when the dissection of this area proves unusually difficult, a wiser and a more expeditious plan is to clamp and divide the external carotid artery at its origin, close its origin by a running stitch of arterial silk and ligate the distal end of the segment (Fig. 58(*c*)) in such a way that the posterior

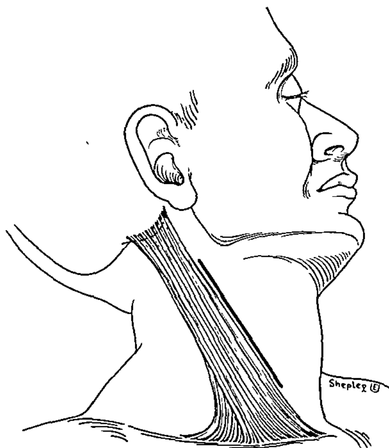


FIG 55.—Line of incision.

part of the bifurcation and the posterior part of the internal carotid artery can be approached more directly. The separation of the adventitia is continued distally for a distance of 2 centimetres on the internal and external carotid arteries. In addition to difficulty caused by the origin of the ascending pharyngeal branch, a low superior thyroid branch may impede the dissection. The object is to strip the whole of the adventitia from an area which includes the distal part of the common carotid and the proximal parts of the internal and external carotids (Fig. 60(*b*)), or, if the external carotid has been divided, of the internal carotid alone.

If it is necessary to carry out bilateral denervation, a similar operation is performed on the opposite side.

The wound is closed by interrupted stitches grasping the skin and platysma.

After-treatment

There is no special precaution to be taken. On one occasion, after bilateral operations, one of us (J. L.) encountered transient weakness of a forearm and hand.

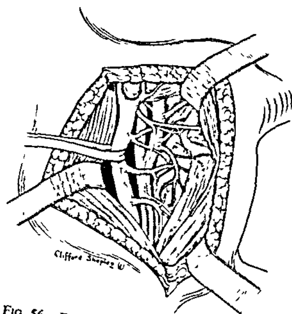


Fig. 56.—Exposure of vascular bundle and isolation of internal jugular vein.

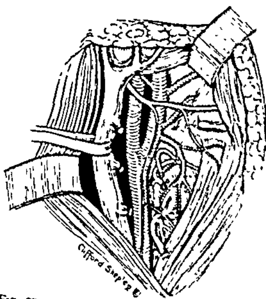


Fig. 57.—Ligation of tributaries of internal jugular vein; definition of descendens hypoglossi nerve.

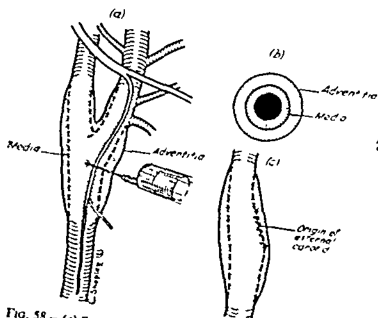


Fig. 58.—(a) Start of subadventitial injection of procaine solution, (b) plane of placement of subadventitial procaine solution; (c) alternative method of dealing with external carotid artery.

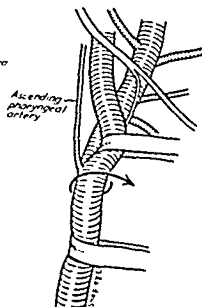


Fig. 59.—Illustrating low origin of ascending pharyngeal artery.

Results

A sufficient number of cases has now been recorded (see, for example, Cattell and Welch, 1947) to establish the operation of denervation of the carotid sinus, when its hypersensitivity has been shown to be the cause of symptoms. Our original patient (Turner and Learmonth, 1948) has been examined at intervals of three months for five years On each occasion firm pressure first over one carotid sinus and then over the other has not influenced the heart's rate, the blood pressure, or the electrocardiogram.

Recurrence of symptoms after operation may be due to one of two causes: (1) that the original operation was incomplete; in such cases the hypersensitivity of a sinus will be found to have returned; and (2) after unilateral operation, the development of hypersensitivity in the opposite sinus. In both sets of circumstances further operative treatment is indicated

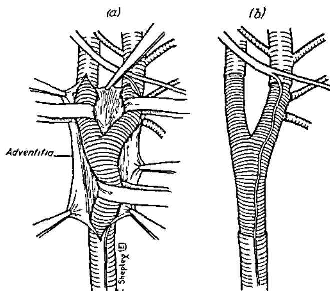


FIG. 60.—(*a*) The dissection in progress. (*b*) The dissection completed.

One of us (J. L.) has observed an unusual case in which—although the carotid sinuses remained insensitive after bilateral denervation—an attack of syncope complicated impaction of faeces in the rectum.

In man, bilateral denervation of the carotid sinuses does not appear to carry the risk of inducing hypertension, an undoubted sequel of the procedures in at least some animals (Heymans, Bouckaert and Regniers, 1933).

It has not as yet been definitely established in man that section of the ramus caroticus of the glossopharyngeal nerve (Ray and Stewart, 1942) is as uniformly effective as the more extensive denervation which we have described in this article.

(*See also British Surgical Practice* Carotid Body, Vol. 3, page 11, S K. 85)

REFERENCES

Askey, J. M (1946). *Amer Heart J*, **31**, 131.
Cattell, R. B, and Welch, M L. (1947). *Surgery*, **22**, 59.
Draper, A. J. (1950) *Ann. intern Med.*, **32**, 700.
Engel, G. L, and Engel, F L. (1942) *New Engl. J. Med*, **227**, 470.
— Romano, J., and McLin, T R. (1944). *Arch. intern. Med.*, **74**, 100.
Ferris, E B, Jun, Capps, R B, and Weiss, S. (1937) *Arch. Neurol Psychiat*, **37**, 365.
Forster, F. M, Roseman, E, and Gibbs, F. A. (1942). *Arch. Neurol Psychiat.*, **48** 957.
Galdston, M, Goldstein, R, and Steele, J. M. (1943). *Amer. Heart J*, **26**, 213.
Hering, H E. (1927) *Die Karotissinusreflexe auf Herz und Gefässe vom normal-physiologischen pathologisch-physiologischen und klinischen Standpunkt.* Dresden: Steinkopf.

Heymans, C., Bouckaert, J. J., and Regniers, P. (1933). *Le Sinus carotidien et la Zone homologue*

McSwain, B , and Spencer, F. C. (1947). *Surgery*, 22, 222.
Nathanson, M. H. (1946). *Arch. intern Med.*, 77, 491.
Ray, B. S., and Stewart, H. J. (1942) *Surgery*, 11, 915.
Rovenstine, E. A., and Cullen, S. C. (1939). *Surgery*, 6. 167.
Sigler, L. H. (1942a). *Arch. intern. Med.*, 70, 983.
— (1942b) *New Engl. J. Med.*, 227, 725.
— (1943). *Arch. intern. Med*, 72, 613.
Stern, J. E. (1938). *J. Amer. med. Ass.*, 110, 1986.
Tanney, A D., and Lilienfeld, A. (1942) *Arch intern. Med*, 16, 676.
Turner, R., and Learmonth, J. R. (1948). *Lancet*, 2, 644
Weiss, S., and Baker, J. P. (1933). *Medicine*, 12, 297.
— Capps, R. B., Ferris, E. B , Jun , and Munro, D. (1936) *Arch. intern. Med*, 58, 407.

THE TREATMENT OF CARCINOMA OF THE COLON

By O. V. LLOYD-DAVIES, M.S (Lond.), F.R.C.S.(Eng.)
Consultant Surgeon, St. Mark's Hospital, London; and the Middlesex Hospital, London

and

C. NAUNTON MORGAN, M B., B.S.(Lond), F.R.C S (Eng)
Consultant Surgeon, St Mark's Hospital, London; and St. Bartholomew's Hospital, London

and

J. C. GOLIGHER, Ch.M.(Ed), F.R.C.S.(Eng.)
Consultant Surgeon, St. Mark's Hospital, London; and St. Mary's Hospital, London

In the section on Carcinoma of the Colon in *British Surgical Practice*, the operations advised are either resections of the Paul-Mikulicz type, or, in the left colon, resections with immediate anastomosis, but only after a preliminary transverse colostomy. The writer of the section, Sir Hugh Devine, recognized that the use of sulphonamide drugs and antibiotics, locally and systemically, might eventually permit of the more direct procedure of resection and immediate intraperitoneal anastomosis without a proximal colostomy This forecast has proved largely correct, though other factors beside chemotherapy and antibiotics have played a part in its realization. We refer to the conditions that have made surgery in general so much safer than it was before World War II; namely to the improvement in transfusion methods, to the greater understanding of the problems of fluid and electrolyte balance, and to the considerable advances in anaesthesia which now give the surgeon ideal operating conditions allowing a much more careful and meticulous operative technique.

As a result of all these factors, resections with immediate anastomosis can at the present time be performed with remarkable safety. Thus, Allen (1950) has recorded a series of 159 cases of carcinoma in various parts of the colon treated in this way with only two hospital deaths Resection with immediate anastomosis and without proximal decompression has been performed in 109 cases of carcinoma of the colon during the last 5 years at St Mark's Hospital, London, with only 3 post-operative deaths, none of which were due to sepsis.

Certain drawbacks attach to the Paul-Mikulicz procedure. Undoubtedly, if it is to be thoroughly radical, it requires a more extensive mobilization of the colon than a resection with direct anastomosis, since the ends of bowel have to be exteriorized without tension. Sometimes this extra mobilization may be difficult to obtain, especially when the growth lies in the lower sigmoid and there is insufficient bowel on the distal side. In the obese subject with a short, fat-laden mesentery there are added difficulties. Under these circumstances, if the surgeon persists in his plan to perform a Paul's type of resection he may compromise his chances of eradicating the disease.

In the average case with a carcinoma of the colon situated elsewhere than in the distal sigmoid, as radical a removal can usually be achieved by a Paul-Mikulicz operation as by an intraperitoneal resection, and the choice of method will depend on the surgeon's personal predilection. Our own feeling is that now the Paul-Mikulicz

Heymans, C., Bouckaert, J. J., and Regniers, P. (1933). *Le Sinus carotidien et la Zone homologue cardio-aortique· Physiologie, pharmacologie, pathologie, clinique.* Paris; Doin.
— and van den Heuvel-Heymans, G. (1950). *Arch. int. Pharmacodyn.*, **83**, 520.
Marmor, J., and Sapirstein, M. R. (1941). *J. Amer. med. Ass*, **117**, 1089.
McSwain, B., and Spencer, F. C. (1947) *Surgery*, **22**, 222.
Nathanson, M. H. (1946). *Arch. intern. Med.*, **77**, 491.
Ray, B. S., and Stewart, H. J. (1942). *Surgery*, **11**, 915.
Rovenstine, E. A., and Cullen, S. C. (1939). *Surgery*, **6**, 167.
Sigler, L. H. (1942a) *Arch. intern. Med*, **70**, 983.
— (1942b). *New Engl. J. Med*, **227**, 725.
— (1943). *Arch. intern. Med.*, **72**, 613.
Stern, J. E. (1938). *J. Amer. med. Ass.*, **110**, 1986.
Tanney, A D., and Lilienfeld, A. (1942). *Arch. intern Med*, **16**, 676.
Turner, R., and Learmonth, J R. (1948). *Lancet*, **2**, 644.
Weiss, S., and Baker, J. P. (1933). *Medicine*, **12**, 297.
— Capps, R. B., Ferris, E. B, Jun, and Munro, D. (1936). *Arch. intern. Med.*, **58**, 407.

procedure no longer has the merit of greater safety, it presents no particular advantage in the non-obstructed case of carcinoma coli, though it may rarely be indicated in patients with a moderate degree of unsuspected subacute obstruction, or as a means of rapidly terminating a difficult and prolonged resection in an unfit patient.

SURGICAL PATHOLOGY

Modes of Spread

Direct spread

Adhesions to other organs and to the abdominal wall are not uncommon with colon carcinomas and may present the surgeon with a formidable fixed mass implicating several viscera. Eradication of the growth will then necessitate excision in part or *in toto* of other adherent organs, or removal of a portion of the abdominal wall. It is important to emphasize that pathological examination of the specimens obtained by such extended resections often shows that spread was much less extensive than was feared at operation; quite frequently lymphatic metastases are few, or entirely absent, and it is not uncommon to discover that the adhesions to adjoining structures are purely inflammatory and contain no growth. In the cases requiring the removal of other adherent organs we have found that only in one-third were the adhesions due to neoplastic involvement.

With thorough local removal in these apparently hopeless cases the prognosis is often quite good. Indeed, with few other carcinomas is courageous surgery more amply rewarded, so that the surgeon should not allow himself easily to be deterred by local fixity of the growth.

Peritoneal spread

Widespread peritoneal deposits will of course render the case quite inoperable, but when such plaques are confined to the immediate vicinity of the growth and there is no ascites it may be possible to excise the affected area of peritoneum *en bloc*, with some slight chance of cure.

Lymphatic spread

Intramural lymphatic spread in the submucous lymphatic plexus beyond the macroscopic edge of the primary growth is apparently a very restricted process as a rule. Only in anaplastic growths—which represent about one per cent of all colon carcinomas—does it occur to any extent, and then malignant cells may sometimes be found in the submucosa many inches away from the growth. In these cases the prognosis is usually very unfavourable even with the most radical excision. In the average case submucous extension seldom proceeds more than one-half to one inch proximal or distal to the growth, so that resection of 2 inches of bowel on either side should ensure adequate clearance. However, almost invariably a much more extensive resection is required for removal of the related lymphatic glands.

Extramural lymphatic spread in connexion with carcinoma of the colon has been very fully studied in the classical researches of Jamieson and Dobson (1907) and Clogg (1908) and more recently has been re-investigated on a much more extensive scale by Dukes (1951) in the Research Department of St. Mark's Hospital. Patho- [illegible] by resection shows that [illegible] r involvement. In the [illegible] uently confined to the paracolic glands and those accompanying [illegible] sels near the growth. Contrary to what is usually believed, there seems to be no significant difference in the frequency of lymphatic metastases found with right and left colon growths.

The lymph glands draining lymph from the site of the carcinoma may be enlarged either from carcinomatous metastases or from septic absorption from the ulcerating

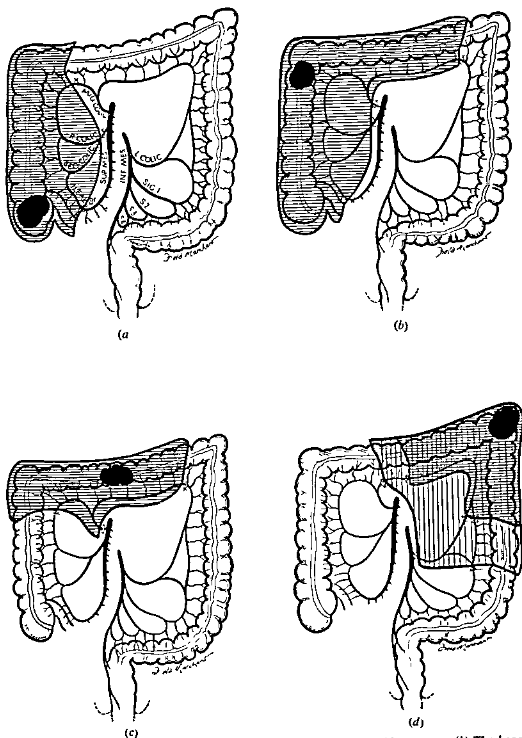


FIG 61.—Diagrams showing extent of resection for carcinoma (a) The caecum. (b) The hepatic flexure (c) The transverse colon (d) The splenic flexure, the inner more darkly shaded area indicating a less extensive excision, the outer the ideal resection

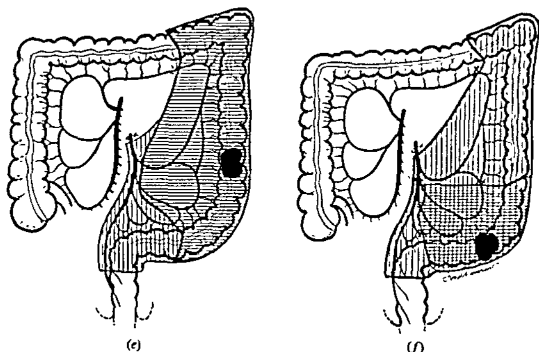


FIG. 61 (*cont.*).—(*e*) The descending colon, the outer more lightly shaded area, including ligation of the inferior mesenteric artery at its origin, being preferable. (*f*) The sigmoid colon, the outer more lightly shaded area, including the inferior mesenteric artery at its origin, being the one now usually favoured.

surface of the growth. Usually, septic glands are softer than malignant ones, but it is quite impossible at laparotomy to distinguish between them with accuracy. Also, early glandular metastases may not be associated with any enlargement or induration; therefore the only safe course is *to remove in the widest possible manner the entire* related lymphatic field.

Venous spread

Hepatic metastases may be palpable on the surface of the liver or may be partly or completely buried in the liver substance, so that the surgeon's decision at laparotomy as to the presence or absence of involvement of the liver may well be inaccurate. Small cysts and simple tumours of the liver may be mistaken on palpation for secondary deposits and inspection may be necessary to establish the true nature of these lesions. If any doubt remains it is best to assume that the liver condition is benign, and observe the patient subsequently for clinical signs of hepatomegaly.

If undoubted liver deposits are present and are apparently confined to the left lobe, it may occasionally be worth removing this lobe at the colectomy operation, or at a second intervention, in the hope that the other lobe may be quite clear. Left lobectomy in conjunction with resection of a carcinoma of the colon or rectum has sometimes been followed by complete cure.

Hepatic metastases may be compatible with survival for a year or more, so that a palliative excision of the primary growth is frequently justified in cases with secondary deposits in the liver.

SURGICAL ANATOMY

Scope of excision required for radical removal of carcinomas in various situations

The extent of resection required for growths in different segments of the colon is determined by the necessity for wide removal of the extramural lymphatics which accompany the main colic vessels supplying the region concerned.

Ideal resections for carcinomas in various parts of the colon are illustrated in Figs. 61(*a–f*).

TECHNIQUE OF COLON ANASTOMOSIS

The general principles of intestinal suture are of course well established, and it is only necessary here to mention the special problems of anastomosis in the colon and to describe a proven and satisfactory technique. The method of closing both ends of bowel after a resection and performing a lateral anastomosis, favoured by some surgeons for both small and large gut, suffers the disadvantages that it is more extravagant in bowel—often a matter of some importance in colon resections where only a limited amount of bowel is available—and that the blind ends are subsequently liable to undergo considerable dilatation, giving rise to discomfort and on occasion perforation. For these reasons end-to-end anastomosis is generally preferred.

In the past peritonitis following upon colon resection induced some surgeons to devise so-called "aseptic" methods of suture—a good review of these is given by Monro (1950). It is of course quite impossible to make any method of anastomosis in the colon completely aseptic, but an aseptic technique may reduce the amount of soiling at the time of operation. This method of anastomosis is founded upon a faulty conception of the factor chiefly responsible for post-operative sepsis, which is not contamination during the operation but subsequent leakage. In our opinion the method of "open" anastomosis, with an inner through-and-through suture and an outer layer of sero-muscular (Lembert) sutures, provides a more secure anastomosis and one less likely to leak than does the aseptic technique with its single row of sero-muscular stitches.

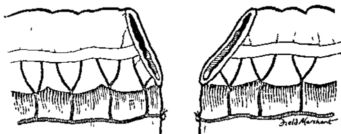
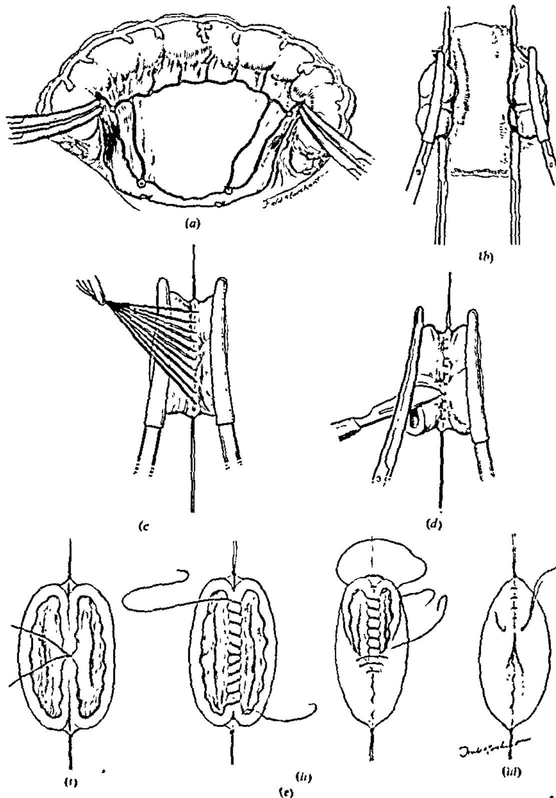


FIG 62—Diagram showing value of oblique line of section of colon to ensure a good blood supply to all parts of the cut edge and a wide lumen at the site of the anastomosis.

In the past the failure of union, and leakage after anastomosis in the colon have been attributed to the high infectivity of the colon contents, to the thinness of the colon wall and to its relatively poor blood supply. With modern intestinal antiseptics the infective factor can be greatly reduced and the thinness of the colon wall calls for a delicate and meticulous technique, employing the finest needles and suture materials.

The blood supply to the large intestine requires special attention owing to its variability. A good supply is provided by the main colic vessels, but the colon can be nourished for considerable distances by the marginal artery alone. For example, after resection of the left colon an anastomosis may not infrequently be carried out between the distal end of the transverse or descending colon—supplied only by the middle colic through the marginal artery—and the upper part of the rectum; but the surgeon must be completely satisfied that the blood supply at the site of proposed anastomosis is adequate.

Though the colour of the bowel and the presence of arterial pulsation indicate a satisfactory blood supply, the only sure guide is the occurrence of arterial bleeding *from the cut edge of the colon at the site of resection. Mass division of the mesentery* may lead to damage of the blood supply at the proposed site of anastomosis with consequent loss of viable bowel; where possible the mesenteric vessels should be individually secured. It is advisable to divide the bowel obliquely in order to obtain



Fi[illegible] [illegible] anastomosis (a) Division of [illegible]

the best possible arterial supply to all parts of the line of section; this also has the advantage of obviating any narrowing of the lumen by the subsequent suturing (*see* Fig. 62). The terminal fringe of colon wall which has been devitalized by the crushing clamp applied during the resection should be excised. This may also decrease the chances of implanting malignant cells in the suture line.

Interrupted stitches probably interfere less with the blood supply to the ends of the bowel than does a continuous suture, and are therefore preferable, at any rate for the outer sero-muscular row. In tying them it is important to avoid excessive force which

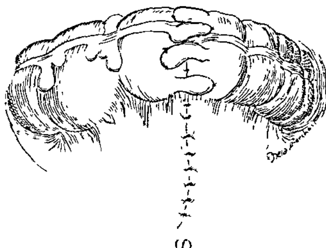


FIG 63 (*cont.*).—(*f*) Completed anastomosis with appendices epiploicae stitched over the suture line, and the gap in the mesocolon closed.

increases the amount of strangulation and necrosis of tissue. As regards suture material, No. 00 serum-proof silk (or fine linen or cotton) is used for the sero-muscular stitches, and a continuous No. 00 atraumatic chromic catgut is employed for the through-and-through suture (Fig. 63(*a*–*f*)).

At all costs it is essential to avoid tension on the site of anastomosis.

TREATMENT OF CARCINOMA OF THE COLON WITHOUT ACUTE OBSTRUCTION

Pre-operative care

Locally, pre-operative care is designed to clear the bowel of faeces retained above the growth, and to sterilize the gut contents by intestinal antiseptics. The former aim is secured as far as possible by administration of mild aperients and lubricants such as magnesium hydroxide and medicinal paraffin and by daily colonic lavage. It must be admitted, however, that if the growth is completely annular and tightly constricting this mechanical cleansing is often ineffective even if prolonged over a longer period than the five to seven days usually set aside for preparation of these cases.

Intestinal antisepsis is secured by giving insoluble sulphonamides such as phthalylsulphathiazole orally for five to seven days, at the rate of ten grammes per day in divided doses; this is supplemented by the oral administration of streptomycin one gramme twice daily for the last two to three days.

In addition to this local preparation the patient's general condition is carefully assessed. If the haemoglobin be below 80 per cent, anaemia and hypoproteinaemia are rectified by pre-operative blood transfusion, by giving iron and by a high protein diet supplemented by protein concentrates. The diet should be high in caloric value but low in residue.

All patients are given vitamin B complex, ascorbic acid and vitamin K to correct any vitamin deficiencies. During this preparatory period the patient need not be

confined to bed but should be active, and in particular should be instructed in respiratory exercises.

If the growth is in a situation where it might become adherent to a ureter, it is as well to have an intravenous pyelogram to show whether in fact the ureter has been implicated and whether the opposite kidney is functioning normally. Such advance information may be helpful to the surgeon in planning his operation.

Finally, an intravenous drip infusion is set up before the operation commences, so that any sudden losses of blood during operation can be rapidly replaced.

Incisions

Adequate access is a prerequisite for good surgery, and is especially important in colon surgery because of the frequency with which carcinomas of the colon necessitate difficult, complicated resections. The optimal approach to different parts of the large bowel is achieved by a combination of the correct incision, the correct position of the patient on the table, and good anaesthesia. For resection of a transverse colon carcinoma right or left paramedian rectus sliding incisions or a transverse incision give good access with the patient in the ordinary supine, horizontal position. For resections of the right or left colon, long right or left paramedian incisions, extending from near the pubis to well into the epigastric region, may be used or an oblique muscle-cutting incision running from near the tip of the last rib medially and downwards to [illegible] an angle of 30° or so with the horizontal. The small gut then gravitates [illegible] dependent part of the abdomen and thus facilitates the mobilization of the colon on the opposite side, especially at the hepatic or splenic flexures. Growths of the sigmoid and recto-sigmoid are best dealt with through a left paramedian incision with the patient in a fairly steep Trendelenburg tilt, preferably whilst maintained in the lithotomy Trendelenburg position by special leg rests (Lloyd-Davies, 1939).

Exploration

Careful systematic exploration to determine the extent and spread of the lesion is first carried out. In order to minimize the risk of disseminating carcinoma cells in the peritoneal cavity, it is probably wise to make examination of the primary growth itself the last step in this exploration. The liver is first palpated, then a hand is passed down into the pelvis to feel for deposits in the pelvic peritoneum. The greater omentum is next inspected and palpated for the presence of tiny "seedling" deposits. As 3·5 per cent of all cases of carcinoma coli have two or more primary growths, it is important th[illegible] additional carcinomas. [illegible] size and fixity; whether it has involved the peritoneal surface [illegible] uced plaques in the adjoining peritoneum; if adherent, to which organs or structures it has become adherent, and whether the related lymphatic glands are enlarged or indurated. The degree of obstruction present should also be noted as it may influence the choice of operative procedure.

Assessment of operability and management of inoperable cases

[illegible] of the colon to [illegible] often preferable to perform a palliative resection [illegible] ave six or nine months of life before him. Our own resectability rate for carcinoma coli is approximately 95 per cent and this includes 15–20 per cent of palliative excisions in the presence of liver metastases. If, however, the growth is quite irremovable or

extensive peritoneal secondaries contra-indicate its removal, a decision will have to be made as to the advisability of a palliative procedure.

If there is a considerable degree of chronic obstruction present and it seems likely that acute obstruction is imminent, steps should be taken to relieve it. When feasible a short-circuiting lateral anastomosis between the bowel proximal and distal to the lesion is the operation of choice, but a proximal colostomy close to the growth may be unavoidable.

Usually in cases with inoperable growths a relieving operation for obstruction is not required, and is to be avoided, especially if it involves a colostomy. Finally, in an inoperable case a biopsy should be obtained for histological examination even when the nature of the condition seems to be beyond all doubt.

Radical resections

Right hemicolectomy

The parietal peritoneum in the paracolic gutter is divided from the caecum to a point just above the hepatic flexure, and the bowel with its medial leaf of peritoneum and colic vessels is elevated from the posterior abdominal wall and mobilized towards the midline. Usually some bands of connective tissue containing a few small vessels have also to be divided on the supero-lateral aspect of the flexure before this portion [illegible]

and right colic vessels are clearly visualized. They should be tied and divided close to their origins from the main superior mesenteric trunk. The incisions made in the peritoneum to divide these vessels are then joined and continued below into the mesentery of the ileum six inches or so from the ileo-caecal junction As it nears the small bowel this incision exposes the communicating vessel between the terminal ileal branches of the superior mesenteric artery and the ileo-colic artery, this is ligated and divided and the ileum severed between crushing clamps.

Attention is now turned to the distal part of the bowel. If the growth is in the caecum or low in the ascending colon it should not be necessary to sacrifice the middle colic artery or resect more than the first three or four inches of the transverse colon. Mobilization of the transverse colon will be enhanced by dividing the gastro-colic omentum, but this is not always necessary for growths in this situation. The great omentum related to the portion of transverse colon being resected is excised with the specimen. The incision in the peritoneum at the site of division of the right colic artery is now prolonged upwards into the transverse mesocolon keeping to the right of the main middle colic vessel and eventually crossing its right branch which turns down to join the ascending branch of the right colic close to the colon (*see* Fig. 61*a*). This communicating branch is divided and ligated and the colon divided between two crushing clamps. If, however, the growth lies in or close to the hepatic flexure it is wiser to tie the main middle colic artery close to the superior mesenteric and to carry the incision in the transverse mesocolon upwards on the left side of this vessel and across the marginal artery between the middle and left colic branches as in Fig. 61*b*. In these cases, of course, an appropriately greater amount of the omentum has to be removed with the colon.

Continuity between the ileum and the colon can be restored in one of four ways: (1) by lateral anastomosis, the ileal and colon stumps being both closed like a duodenal stump in a gastrectomy and an iso-peristaltic side-to-side anastomosis established; (2) by side-to-end anastomosis, the ileum being closed and its side joined to the open end of the colon; (3) by end-to-side anastomosis, the colon being closed and the end of the ileum implanted into its side, and (4) by end-to-end anastomosis, the preferable

method; the disparity in the calibres of the small and large bowel being overcome by more oblique section of the ileum than the colon. Whichever technique is used the gap between the cut edge of the ileal mesentery and the transverse mesocolon is finally closed by [illegible]

rig[illegible] establishing ileal drainage and is primarily intended for resections in the presence of acute or subacute obstruction. A catheter with multiple holes is passed through a side-to-side or end-to-side (ileum to colon) anastomosis well into the lower ileum and brought out through one edge of the invaginated end of the colon which is then again invaginated around the emerging tube. The end of the catheter is now drawn through a small incision in the abdominal wall immediately overlying the anastomosis, and adjacent appendices and the colon are sutured to the parietes at this point (*see* Fig. 64). A skin suture fixes the catheter.

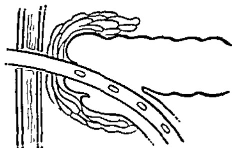


Fig. 64.—Diagram illustrating Muir's method of ileo-transverse colostomy with decompression of terminal ileum.

The advantage of this method is that it provides decompression of the ileum above the anastomosis by gentle suction applied to the catheter, and this protects the suture lines from dangerous tension and minimizes the risk of paralytic ileus. When the catheter is finally withdrawn after 7–14 days the resulting fistula rapidly closes.

Resection of the transverse colon

The first step consists in the division of the gastro-colic omentum above or below the gastro-epiploic arcade along the greater curvature of the stomach for a distance corresponding to the proposed extent of the resection (*see* Fig. 61*c*). The great omentum is divided on either side to reach the colon at the sites of its proposed division, thus leaving the bulk of the omentum attached to the piece of bowel which is going to be removed. It now only remains to divide the colon and mesocolon, taking out a portion of the marginal artery with related paracolic glands and also preferably the stem of the middle colic vessels. The operation is completed by end-to-end anastomosis between the hepatic and splenic ends of the transverse colon, and, to avoid tension at the suture line, it will be necessary to mobilize the colic flexures and the upper parts of the ascending and descending colon.

Resection of splenic flexure and descending colon

The mobilization of the colon here proceeds exactly as in a right hemicolectomy, but the splenic flexure, lying as it does at a higher level than the hepatic, is more difficult to free.

The approach to the flexure itself will be greatly assisted if the incision of the peritoneum in the paracolic gutter and the division of the gastro-colic omentum are carried out first. The two freed limbs of bowel—ascending colon and transverse colon—are then held in the left hand whilst an assistant exposes the flexure with a deep retractor. A few small vessels in the phrenico-colic ligament may require ligating and care must be taken not to damage the spleen. When mobilizing the iliac and

the descending colon the same care must be taken as on the right side to displace the ureter and spermatic or ovarian vessels posteriorly.

The omentum is divided so that a generous portion of it remains attached to the segment of transverse colon which it is proposed to remove. The extent of the resection to be carried out depends on the precise situation of the growth. If this lies at the flexure itself it should suffice to remove six or eight inches of transverse colon together with the descending colon down to and including the left colic artery. If it is situated in the distal end of the transverse colon the resection should be extended proximally to embrace the stem of the middle colic vessels as well, or if low down in the descending colon or in the iliac colon carried distally to include the first and second sigmoid arteries. The transverse and iliac or sigmoid colon are anastomosed end-to-end, both pieces of bowel being mobilized as much as is necessary to secure easy approximation without tension.

Resection for carcinoma of the sigmoid

The first step in any resection involving the sigmoid colon is a thorough separation of the lateral aspect of the iliac segment and its mesocolon from the parietal peritoneum of the left iliac fossa, to which they have normally become adherent during development, making the iliac colon a "fixed" part of the large intestine. Once these developmental adhesions have been severed, preferably by scissors dissection, the whole sigmoid loop has its natural mesocolon "restored" to it, and if held up to the light the vascular pattern can be studied and the extent of the resection decided upon. This may be relatively restricted involving removal of two or three of the sigmoid branches up to their origin from the inferior mesenteric artery, but leaving the latter vessel intact, as is often advised. It is better, however, to carry out a more extensive excision with resection of the inferior mesenteric trunk itself just below the origin of the left colic artery (*see* Fig 61*f*). This necessitates extending the resection as far distally as necessary to ensure a good blood supply from the middle haemorrhoidal vessels below and to divide the superior haemorrhoidal vessels at this level, usually just below the sacral promontory. Restoration of continuity is achieved by end-to-end anastomosis, the only unusual feature about this being the fact that the presence of appendices epiploicae on the sigmoid colon may interfere with the accurate placing of sutures in the bowel wall If the appendices are broad and bulky it may be advisable to ligate and remove a few of them in order to facilitate the anastomosis. On the other hand, they make a convenient additional cover for the suture line in the bowel after this has been completed so that it is best to retain as many as possible.

With carcinomas of the lowest part of the sigmoid colon it is important to ensure that the lo[illegible] should be accurately measured at the time.

In all instances the open ends of the bowel to be anastomosed should be swabbed with 1 500 perchloride of mercury to destroy free cells, and the lumens should be examined for the presence of adenomas which should be removed before the through-and-through suture is commenced.

Closure of the wound

The parietal wound is sutured in layers with continuous or interrupted catgut, silk, linen, nylon or stainless steel wire. Though we have had occasional disruptions and herniations after the use of all these suture materials it is our impression that they are rather less common with non-absorbable sutures. The site of the anastomosis is usually drained through a separate incision using corrugated rubber, and where

possible this is placed retroperitoneally, or in such a position that small gut c become adherent.

Post-operative care

Post-operative care does not differ materially from that given after any : abdominal operation involving opening of the alimentary tract. *Antibiotics* su penicillin or streptomycin are administered systemically for 4–5 days. After the e of the anaesthetic have passed the patient is allowed to assume whatever positi finds most comfortable, usually with the head and chest *slightly raised. Active* r ments are encouraged, respiratory exercises are given thrice daily, if necessary ceded by a sedative to minimize the pain in the first few days. On the second or evening the patient is usually helped out of bed for a few minutes whilst the b made; thereafter ambulation is gradually increased. The legs are examined eacl for evidence of venous thrombosis, and if calf tenderness or painful limitati dorsiflexion of the foot develops anticoagulants are given. The intravenous infusion commenced before the operation is continued until flatus is passed abdomen is quite flat and normal peristaltic sounds are audible, the abdomen l examined and auscultated night and morning. An isotonic solution is used conta 20 per cent normal saline and given at the rate of 2,500–3,000 millilitres per depending upon the size and weight of the patient. A careful check is kept upo fluid intake and output and the urinary chlorides estimated at each voiding. S quantities of fluid may be given by mouth from the beginning, but any sign of ga *distension is immediately relieved by the passage of a No. 7 or 8 (English) oesoph:* tube and the institution of intermittent or continuous gastric suction. If ileus o the intravenous infusion is continued and in addition to the normal basic allow of 20 per cent normal saline, *fluid and electrolytes must be given to compensat* the losses by gastric suction. The appropriate replacing fluid can best be determ by ascertaining the ionic content of the aspirate, or, if laboratory facilities do permit, it is usually safe to replace with equal quantities of normal saline. If ga aspiration and intravenous fluids have to be continued for several days it is desi also to provide potassium-chloride in the infusion (3 grammes daily), but this sh only be given if there is a free diuresis. If no difficulties with ileus arise, the m feeds are gradually increased and slowly built up into a light diet.

A flatus tube is passed periodically from the second day and usually flatus is pa spontaneously about the third or fourth day. The bowels act a day or so later their action may be encouraged by giving a glycerine suppository per anum.

Wound drains are shortened on the third day but retained for a full seven day as to establish a definite track down to the site of anastomosis along which any fa leak from the suture line may escape to the surface. Skin sutures are removed on eighth to tenth day.

The question arises as to whether a proximal decompressive vent should be es lished in the form of a transverse colostomy or caecostomy. In recent years we h used such safeguards only if the anastomosis *has presented special difficulties*, as, example, when a low sigmoid carcinoma has been resected in an obese patient wi narrow pelvis, or should there be any doubts whatsoever about the anastomo Under these circumstances we have very occasionally employed *a temporary tr* verse colostomy for a fortnight or so

TREATMENT OF CARCINOMA OF THE COLON WITH ACUTE OBSTRUCTION

Some degree of chronic intestinal obstruction is almost the rule with carcinoma the colon, but as a result of oedema, impaction of a faecal mass in the strictu portion of bowel or intussusception of the growth, acute intestinal obstruction n

supervene. This emergency calls for separate consideration, for when a carcinoma has caused acute obstruction immediate resection is attended by special difficulties and dangers.

The patient's general condition may be such as to render him unfit for a major operation. The highly septic nature of the contents of the obstructed colon, unchecked by any form of pre-operative intestinal antisepsis, the oedematous friable condition of the bowel wall making it unsuitable for intestinal suture, and the greatly distended state of the colon, which may render operative manipulations in the abdomen unusually difficult, combine to increase the hazards of primary resection in these cases.

It is accepted as a general rule that in operating upon such cases the surgeon's prime objective is to relieve the obstruction by proximal colostomy, caecostomy, or enterostomy, or in certain cases by a short-circuiting anastomosis. The eradication of the growth and its lymphatic field is best reserved for a later operation. The drainage opening should be established in a situation where it will not interfere with the conduct of the second operation. Occasionally, relief of the obstruction in the right colon can best be achieved by immediate resection. These points will be made clear later in the detailed account of the management of colon carcinoma with obstruction.

Clinical assessment and pre-operative care

The general condition of a patient with obstruction due to carcinoma of the colon is often quite good, because vomiting, with its resulting dehydration and electrolyte imbalance, is usually a late phenomenon.

Obstruction in the left colon may produce very considerable distension of the colon, but if the ileo-caecal valve is competent the small gut may not be at all dilated. Even with growths in the right colon the valve may at first protect the ileum from distension.

A plain x-ray examination of the abdomen is of the greatest possible value in diagnosis and in determining the exact site of the neoplasm. It will show whether there is gaseous distension of the large bowel, and careful observation of the distal extent of this gas shadow will localize the lesion with fair accuracy. Sometimes, however, with obstructing growths in the sigmoid colon the distension of the descending colon is not well shown and an erroneous diagnosis of carcinoma of the splenic flexure may be made. In volvulus of the sigmoid, which is a possible source of confusion in diagnosis, x-ray examination usually demonstrates clearly the grossly dilated sigmoid loop and avoids error. Generally, the plain film gives all the information that is required.

An attempt is made in the first instance to relieve the obstruction by soap and water enemas which may occasionally be effective, particularly if the growth is located in the sigmoid. Sigmoidoscopy may give valuable information and on rare occasions allow the passage of a rubber catheter through the obstruction.

Certain pre-operative measures are necessary. Dehydration and electrolyte depletion if present should be corrected by intravenous therapy, and it is a wise precaution in all cases to have an intravenous infusion commenced before operation. When vomiting is a symptom, or if the x-ray examination reveals gaseous distension of the small gut, it is imperative to pass a Ryle's tube, or better, a small soft No. 7 or 8 English gauge oesophageal tube to empty the stomach and avoid regurgitation of gastric contents during induction of the anaesthetic. Long gastro-intestinal tubes, such as the Miller Abbott or Cantor tube, are unsuitable in these emergency cases because of the time required to induce them to negotiate the pyloric sphincter and upper intestinal tract. Furthermore, decompression of the small gut usually has no influence on the distension of the large gut and therefore cannot obviate the necessity for operative treatment. Once dehydration and electrolyte loss have been adequately corrected further delay in submitting the patient to operative treatment is to be deprecated.

Choice of operation in acute obstruction

For obstructed growths in the sigmoid or descending colon or at the splenic flexure, undoubtedly the most satisfactory procedure is a loop transverse colostomy established in the right subhepatic region. In this situation it is out of the way of the left paramedian incision that will probably be employed for the resection operation. Also, as the colostomy is close to the hepatic flexure, it should not interfere with the mobilization, resection and anastomosis of the colon at the second operation except possibly when the growth is at the splenic flexure, in which case it may be better to make a caecostomy. A transverse *colostomy completely "defunctions" the distal colon and* permits of irrigations being given from the abdominal opening to the anus to wash out retained faeces and leave the colon clean and collapsed for the resection.

The place where the colostomy should not be placed is just proximal to the growth, as, for example, in the iliac colon immediately above a sigmoid carcinoma, unless the surgeon is absolutely certain that the lesion is quite inoperable, since in this situation a colostomy is a severe handicap to subsequent resection. It must be emphasized that it is difficult to assess with accuracy the fixity of a growth during an emergency laparotomy for acute obstruction and it is well to err on the side of optimism. Sometimes carcinomas seem to become less fixed after the obstruction has been relieved. It has also to be borne in mind that the emergency operation is often performed by a relatively inexperienced surgeon whose standards of operability may be much lower than those of someone of more experience who may be available to undertake the subsequent resection. A verdict of inoperability at the first operation could be justified, *therefore, only by the grossest manifestation of spread, such as extensive peri*toneal deposits wide of the growth itself. It is well to remember too that even hepatic deposits may be compatible with a later palliative resection which would save the patient from the sentence of a colostomy for his remaining year or so of life.

For carcinomas of the splenic flexure or transverse colon causing acute obstruction a proximal transverse colostomy is unfortunately not satisfactory because it will interfere with the subsequent operation for resection of the growth. When the carcinoma is in the middle of a loop of transverse colon without gross intestinal distension, it may be feasible to carry out a Paul-Mikulicz type of resection, but in the average case, especially if the growth lies in the region of the splenic flexure, it is probably wiser to avoid an immediate resection and to perform a caecostomy. In recent years it has been the fashion to decry this operation, and undoubtedly it is less satisfactory as a rule than a colostomy as a preparation for colon resection, but in dealing with a lesion in this situation we consider that caecostomy is the best available operation.

By means of frequent irrigations through the caecostomy—every 2–3 hours—it is possible over a period of 10–14 days to clean and decompress the colon on the proximal side of a growth of the transverse colon or splenic flexure, and by the use of locally acting antibiotics to *render it suitable for a resection with anastomosis.*

For obstruction due to growths of the right colon there has been much controversy as to the correct emergency procedure. It is frequently advised that an anastomosis should be performed between the lower *ileum and the transverse colon to short*-circuit the obstruction; but this procedure involves the same amount of intestinal suturing as does a right hemicolectomy and may present some dangers which the [illegible] If the ileocaecal valve is competent, as is *often the case, then* [illegible] that the anastomosis in a short-[illegible]ted, small bowel and collapsed transverse colon, and should not present any special hazards. *Under these circum*stances a right hemicolectomy with ileo-transverse colostomy will be equally safe, and perhaps more so because if the ileo-caecal valve is competent a lateral anastomosis between ileum and transverse colon may not relieve *the distension of the caecum* which may proceed to perforation. It is therefore considered that a right hemicolectomy

is the operation of choice in these cases unless the surgeon is dealing with a very fixed growth with much pericolic inflammation or suppuration which will probably make resection difficult and dangerous.

If the ileo-caecal valve is incompetent and there is moderate dilatation of the small gut an immediate hemicolectomy is still preferred where possible using Muir's technique for the actual anastomosis between ileum and colon, previously described (*see* page 80).

If there is very gross distension of the small gut any form of anastomosis is hazardous; a right hemicolectomy by Devine's extraperitoneal technique (right-sided Paul-Mikulicz operation) may be performed, but if the amount of intestinal distension proves a serious handicap or the patient's condition is too grave to permit of this operation being carried out, an ileostomy is probably the best procedure.

In this operation the lower ileum is divided 12 inches or so from the caecum, and both ends are brought to the surface through separate incisions. A small Paul's tube is tied into the proximal end For the more seriously ill patients of this type, when the obstructing growth is at, or close to, the hepatic flexure, many surgeons would employ a caecostomy in the first instance, but this makes the subsequent right hemicolectomy more difficult.

Operative procedure

If the growth has not been accurately located pre-operatively it is better to open the abdomen by a small right paramedian incision opposite the umbilicus. If the carcinoma is found on exploration to lie in the left colon the incision is extended upwards slightly and a transverse colostomy established in its upper end. If, however, it is situated elsewhere in the colon the wound is enlarged upwards and downwards as required to provide sufficient access for a right hemicolectomy, or closed and a separate incision made for the performance of a caecostomy.

If the clinical and radiological examinations have definitely located an obstruction at or distal to the splenic flexure, a small upper right paramedian incision is made splitting the fibres of the rectus muscle. A hand is gently inserted to confirm the site of the growth and the state of the liver.

A loop of transverse colon as near to the hepatic flexure as possible is brought out of the wound In cases with gross distension it may be necessary to deflate the bowel with a large-bore needle attached by rubber tubing to a sucker, the puncture in the bowel being afterwards closed with a purse-string suture. The great omentum attached to the loop is gently stripped towards the mesocolon sufficiently to leave the projecting colon bare A glass rod is then passed through the mesocolon to support the bowel above the skin level, and the wound closed round the bowel. Portions of rubber tubing are passed over the ends of the rod to prevent it slipping out, and to prevent the colon extruding itself further the rod is strapped to the abdominal wall. No sutures are passed between the bowel and the parietes or between the two limbs of the loop. Finally, when the wound has been closed and sealed by dressings, an opening is made on the top of the loop and a large Paul's tube tied in place.

Technique of caecostomy

A muscle-splitting incision is made over the distended caecum and the peritoneum is opened. The grossly distended caecum may be easily ruptured and should not be handled. A large-bore needle to which is attached a length of rubber tubing is inserted to decompress the gas within the caecum.

The partially deflated caecum is now packed off and a curved clamp, such as Taylor's, applied to avoid any faecal leak A purse-string suture of No. 0 chromic catgut is inserted around the indwelling needle, which is then removed, and the small puncture hole enlarged to admit a self-retaining catheter about the size of a little finger

(de Pezzer, with the tip removed). The purse-string suture is immediately tied and its end passed through the wall of the catheter to fix it in position. Another purse-string suture is now inserted and drawn tight whilst the caecal wall is invaginated by pushing the tube towards the lumen (Kader-Senn method). A further purse-string suture may be used to increase the invagination. The ends of the final suture are passed through the edges of the parietal peritoneum in order to fix the viscus. The abdominal wall is closed and the tube further secured to the skin by tying one of the skin sutures around it.

(*See also British Surgical Practice*. Colon, Vol. 3, page 103, S. Key 98.)

REFERENCES

Allen, A. W. (1950). *Ann. R Coll Surg. Engl.*, 7, 173.
Clogg, H. S. (1908). *Lancet*, 2, 1007.
Devine, H (1950). *British Surgical Practice*, Vol. 3, p 103. London; Butterworth.
Dukes, C E (1951). *Med Pr*, 5872, 513.
Jamieson, J K, and Dobson, J F. (1907) *Lancet*, 1, 1137.
Lloyd-Davies, O. V. (1939) *Lancet*, 2, 74
Monro, A K. (1950). *Techniques of British Surgery*. Philadelphia; Saunders.
Muir, E F. (1947). *Proc. R. Soc Med*, 40, 831.

CHRONIC CONSTRICTIVE PERICARDITIS

By OSWALD S. TUBBS, F.R.C.S
THORACIC SURGEON, ST. BARTHOLOMEW'S HOSPITAL,
SURGEON, BROMPTON HOSPITAL, LONDON

DEFINITION

In defining chronic constrictive pericarditis in the original article (*see British Surgical Practice*, Volume 4, page 417), it was stated that the heart was normal in size and structure. Although this is usually true it is now realized that enlargement of the heart is not exceptional, a fact emphasized by Paul, Castleman and White (1948) who found moderate or gross enlargement in one-third of their 53 cases. Further, there may be considerable atrophy of the myocardium in patients of relatively advanced years and in those with gross calcification (McKusick, 1952). Paul found degenerative changes in the myocardium in 5 of the 16 cases which came to autopsy.

AETIOLOGY

Tuberculosis remains the only known common cause of constrictive pericarditis, but the frequency with which it can be proven to be the cause varies greatly in recently published series, from 17 per cent of the cases published by Paul and his colleagues (1948) to "the majority" of 45 patients reported by Sellors (1948)

PATHOLOGY

Hitherto the secondary pathological effects of constrictive pericarditis have been regarded to be those associated with stasis in the venous return to the right side of the heart, but White and his colleagues (1948), Scannell, Myers and Friedlich (1952) and others have shown that there is also constriction of the left side of the heart and, consequently, there is at least some degree of pulmonary congestion

CLINICAL PICTURE

A more careful analysis of the clinical picture has revealed that dyspnoea is both the most common and earliest symptom (Mortensen and Warburg, 1948) this symptom has probably escaped attention in the past because the breathlessness is not usually severe and the patients are rarely orthopnoeic. Transient loss of consciousness on effort is another quite common symptom which has previously received little attention. McKusick (1952) suggests that this syncope is due either to failure of the heart to increase its output sufficiently to cover the increased demands, or to cerebral venous pressure changes comparable to the Valsalva manoeuvre.

It is now generally recognized that a correct diagnosis of constrictive pericarditis may be made in the absence of some of the signs classically associated with this condition. For example, the cardiac impulse is not necessarily diminished, for the pericardium over the apex of the heart may almost escape the effects of the chronic inflammatory process. Likewise the blood pressure and pulse pressure, although usually diminished, may be normal: in 25 clear-cut cases, Mortensen (1948) found the highest pulse pressure to be 40 millimetres of mercury, the lowest 20 and the average

30. The heart is commonly of normal size, but may be enlarged as has already been mentioned. More careful study of the heart sounds (which are commonly reduced in volume) has shown that there is frequently a third heart sound or mid-diastolic murmur which McKusick (1952) considers to be due to rapid ventricular filling early in diastole or to a sudden termination of ventricular filling. In addition the pulmonary second sound may be increased due to a raised pulmonary pressure consequent to constriction of the left side of the heart.

SPECIAL AIDS TO DIAGNOSIS

McKusick (1952) has pointed out that widening of the superior mediastinal shadow to the right is almost invariably present in the straight skiagram due to distension of the superior vena cava. Considerable enlargement of the heart shadow can no longer be regarded as strong evidence against the diagnosis of constrictive pericarditis. Electrocardiography has shown that auricular flutter or fibrillation may replace sinus rhythm.

Cardiac catheterization

Cardiac catheterization is a new method of investigation which has proved of value in reaching a diagnosis in difficult cases (Hansen, Eskildsen and Gotzsche, 1951; McKusick, 1952; Scannell, Myers and Friedlich, 1952). Pressure curves taken in the right ventricle have invariably shown an early diastolic fall followed by a rapid rise to an elevated end-diastolic level which is then maintained through the rest of diastole. There is, in fact, a "plateau" in the curve during the latter part of diastole, presumably because the ventricle has already filled to its maximum capacity. If the catheter is advanced along the pulmonary artery into the periphery of the lung, a raised pulmonary capillary venous pressure is commonly found, indicating constriction of the left side of the heart.

DIFFERENTIAL DIAGNOSIS

[illegible] mitral [illegible] carditis can very closely simulate mitral stenosis, due to the small capacity of the [illegible] ventricle. On rare occasions the characteristic auscultatory and cardiodynamic changes [illegible] by the [illegible] hed by [illegible] increase with the heart rate, whereas in constrictive pericarditis the output usually varies directly with the rate.

SURGICAL TREATMENT

Indications

Age considerations

[illegible] much calcification, is [illegible] ccess- [illegible] cases [illegible] the need for surgical relief must be very pressing.

Pericardiectomy in tuberculous pericarditis

The most controversial subject is the place of pericardiectomy in known active tuberculous pericarditis. Holman and Willett (1951) favour very early operation, as

they consider that "tuberculous pericarditis: culminates almost invariably in great thickening and fibrous contraction of the diseased pericardium". The follow-up study (Carroll, 1951) of 71 cases of tuberculous pericarditis suggests that Holman holds an excessively pessimistic view of the prognosis. There is, however, no doubt that most surgeons are now prepared to accept many more cases for pericardiectomy before the infection in the pericardium has become completely quiescent. For example, Santy, Bérard and Piquet (1946) stated that it was necessary to wait for any "evolutive manifestation" to disappear completely before surgical intervention, but Gonin, Froment and Gravier (1951) report 7 cases in Santy's clinic operated on during the active phase with six good results and only one death. The use of streptomycin combined with PAS in preparing the patient for operation, and as an "umbrella" during convalescence from surgery, has undoubtedly had a strong influence in producing good results. Most British surgeons would probably feel that conservative treatment (including anti-tuberculous chemotherapy and pericardial aspiration when required to relieve tamponade) should be continued as long as there is progressive improvement, but that pericardiectomy should be undertaken if cardiac compression persists in the face of conservative treatment.

Pericardiectomy in the presence of bilateral constrictive pleuritis

Constrictive pericarditis is occasionally seen associated with bilateral constrictive pleuritis. Such cases have in the past been considered unsuitable for pericardiectomy, but Overholt and his colleagues (1952) successfully operated on such a patient by performing a left pulmonary decortication at the time of excising the pericardium, and subsequently carried out a decortication of the right lung.

Technique

The operative technique has been modified in recent years because it became clear that incomplete relief of the constrictive syndrome subsequent to operation was not uncommon and was invariably due to inadequate decortication of the heart. It is now generally recognized that the operation should aim at removing the pericardium from the anterior surface of the heart and from both its right and left sides; the heart should also be separated from the diaphragmatic pericardium and the latter excised as far back as possible. Holman and Willett (1949) have found constriction of the venae cavae in many cases and they lay great stress on the importance of freeing the vessels. Holman's experience in this regard is probably exceptional, for Paul, Castleman and White (1948) only once found constriction of the great veins in 42 patients treated surgically. Further, in cardiac catheter pressure readings in 5 patients, Scannell, Myers and Friedlich (1952) found a "marked elevation of right ventricular end-diastolic, right atrial and peripheral venous pressures to a virtually uniform level. This finding immediately rules out constriction of the great veins as a significant factor."

Median sternotomy

Median sternotomy has become the most favoured method of exposing the pericardial sac now that the necessity for very wide excision of the pericardium is appreciated (Holman and Willett, 1949; Welti, 1951). Some surgeons divide the sternum for its entire length [illegible]

[illegible] a left antero-lateral transpleural incision in the fourth intercostal space with division of the fourth and fifth costal cartilages He states that both the right as well as the left side of the heart can be approached through this incision. As there is often considerable post-operative exudation of blood from the cut edges of the pericardium it is highly desirable, whatever approach is used, to make a wide opening between the

space around the heart and one pleural cavity; the latter is then drained for a day or two through an intercostal catheter connected to a water-seal bottle.

RESULTS OF TREATMENT

It is now recognized that persistence of ascites after operation is more likely to be the result of inadequate removal of pericardium than of cirrhosis of the liver. Holman and Willett (1949) also state that relief from the chronic tamponade syndrome should start immediately following surgery and that slow improvement is indicative of an inadequate operation.

With regard to the overall results, Holman and Willett (1949) collected from the literature 265 cases treated by pericardiectomy and found that the results recorded in 257 of these patients showed that 27 per cent died as a result of the operation, a further 10 per cent had died later, 17 per cent were improved and 46 per cent were completely relieved.

(*See also British Surgical Practice*: Heart and Pericardium, Vol. 4, page 412, S. Key 179.)

BIBLIOGRAPHY

Blalock, A. (1952). "Introduction to Series of Papers on Chronic Constrictive Pericarditis." *Johns Hopk. Hosp. Bull.*, 90, 1.

Carroll, D. (1951). "Streptomycin in the Treatment of Tuberculous Pericarditis." *Johns Hopk. Hosp. Bull.*, 88, 425.

Gon [illegible]

Han [illegible]

Holr [illegible]

— and Willett, F. (1949). "The Surgical Correction of Constrictive Pericarditis." *Surg. Gynec. Obstet.*, 89, 129.

— — (1951). "Treatment of Active Tuberculous Pericarditis by Pericardiectomy." *J. Amer. med. Ass.*, 146, 1.

McKusick, V. A. (1952). "Chronic Constrictive Pericarditis. I. Some Clinical and Laboratory Observations." *Johns Hopk. Hosp. Bull.*, 90, 3.

Mortensen, V., and Warburg, E. (1948). "Chronic Constrictive Pericarditis." *Acta. med. scand.*, 131, 203.

Overholt, R. H., Burwell, C. S., Woodbury, J. W., and Walker, J. H. (1952). "Constrictive Peri- [illegible] Pericardiectomy and Pulmonary Decortication."

[illegible] "Chronic Constrictive Pericarditis. A Study of 53

[illegible] Traitement Chirurgical de la Péricardite Constric-

[illegible] ...ension

[illegible] *J.*, 41,

431 [illegible] ...ves. Avantages de la sternotomie

[illegible] ...48) "Chronic Constrictive Peri-

[illegible]" *Amer. J. Med. Sci.*, 216, 378.

FLUID AND ELECTROLYTE BALANCE

By A. W. WILKINSON, Ch.M., F.R.C.S.Ed.

Senior Lecturer in Surgery, University of Aberdeen; Assistant Surgeon, Aberdeen Royal Infirmary and Royal Aberdeen Hospital for Sick Children; Formerly Lecturer in Surgery, University of Edinburgh; Assistant Surgeon, Deaconess Hospital, Edinburgh

INTRODUCTION

Water is the largest single constituent of the human body and all metabolic processes take place in a watery medium. Therefore, it is not surprising that changes in the content and distribution of water in the body cause serious disturbances of function. Some knowledge of the physiology of water and the electrolytes on which its distribution depends is essential for the understanding and treatment of water loss, oedema, acidosis and alkalosis, shock, and for the replacement of losses of gastro-intestinal secretions.

It has become necessary to revise certain previously accepted beliefs such as that in the almost complete impermeability of the cell membrane to sodium and potassium, and in the constancy of composition of the cell substance. A more dynamic conception of the state of equilibrium which exists between intracellular and extracellular fluids has changed the physiological background against which replacement therapy must be planned, but our knowledge of even the common disturbances of body-fluid equilibria is still incomplete.

Until comparatively recently, because of the difficulty of the chemical techniques required, measurements of the sodium and potassium concentrations in biological fluids had seldom been carried out except as part of research programmes. The application of the principle of flame photometry made such measurements easier and much more rapid, but the immediate danger is that the convenience of this method may lead to its over-enthusiastic and uncritical use

APPLIED PHYSIOLOGY OF BODY FLUIDS

Relationship between body water and fat

It has been customary to assume that the quantity of water in the human body is a fixed proportion (70 per cent) of the total body-weight, without taking into consideration the degree of fatness of the individual. As the result of studies on naval divers, Behnke [illegible]
three c[illegible]
compo[illegible]
minimum of structural fat—and named this the "lean body mass" When storage fat is superimposed on this basal structure, body-weight increases, the percentage of water in the whole body decreases, but the lean body mass undergoes surprisingly small changes (Moulton, 1923; Widdowson, McCance and Spray, 1951). *In the com*position of the body fat is thus an important variable, especially as it may vary within wide limits from less than 10 per cent to 50 per cent or more of the total body-weight. In excessively obese subjects body water may amount to less than 40 per cent of total body-weight. Although the composition of the fat-free portion is unaltered, such wide

variation in fat causes great changes in whole body composition when this is expressed as a percentage of total body-weight.

When fat disappears in under-nutrition, it seems to be replaced in part by extracellular fluid, the volume of which may be greatly increased in malnourished persons (McCance, 1951). At the same time, however, malnutrition causes changes in lean tissue composition such as reduction in potassium and nitrogen content.

The inverse relationship between total body water and fat has important clinical applications. Plasma volume and extracellular fluid volume are respectively equal to about 7 per cent and 28 per cent of total body water (Table I); estimates of these volumes based on calculation from body-weight, without regard to the degree of fatness of the individual, may be very misleading in fat persons. McCance and Widdowson (1951) have suggested that the ideal weight of the individual based on his height should be taken as the figure on which such calculations of body water and plasma and extracellular fluid volumes are based. There is now abundant evidence that total body water amounts to only about 60 per cent of this ideal body-weight.

TABLE I

PARTITION OF BODY WATER

	Total body water %	*Ideal body-weight* %	*Volume, 70 kg. adult (litres)*
Total body water	—	60·0	42
Intracellular fluid	70·0	42·0	30
Extracellular fluid	28·0	16·8	12
Interstitial fluid	21·0	12·6	9
Plasma volume	7·0	4·2	3

The content and distribution of body water

In the living organism water does not exist in a free state in the sense that it is unattached, but as water of hydration it forms part of the complex ionic equilibria which make up cell substance and the body fluids. The total quantity of water in the body depends on the total quantity of basic ions, because these determine the body content of acidic ions and therefore the water associated with these ions. The most important basic ions are sodium and potassium, and the distribution of water is governed largely by that of sodium and potassium between the cells and the surrounding fluids. In a lean man weighing *70 kilograms (11 stones) there are about 150* grammes (3 900 mEq.) of potassium, of which 2 per cent is extracellular and 98 per cent [illegible] the bones and therefore relatively inactive. By combining these [illegible] potassium with those for [illegible] body water can be made into [illegible] water forms part of the protoplasm of the cells, is associated [illegible] m (98 per cent of the total body content) and is equal in quantity to about 70 per cent of total body water (Table II).

Extracellular water is associated mainly with sodium, contains only a very small quantity of potassium, forms the environment of the cells and is equal to about 28 per cent of total body [illegible] extracellular water may be further subdivided into interstitial and [illegible] The interstitial fluid occupies the space outside [illegible]

the vessels and between and around the cells, is equal in volume to 21 per cent of body water and forms the immediate environment of the cells. The intravascular fluid, plasma, is situated within the blood vessels and is equal in volume to only 7 per cent of body water. Apart from a large difference in protein concentration there are only small differences in chemical composition between interstitial and intravascular fluid.

TABLE II

PARTITION OF BODY FLUIDS AND ELECTROLYTES
(70 kg. man (11 st. or 154 lb.))
(Total body water = 60 per cent body-weight = 42 litres)

	Extracellular fluid		*Intracellular fluid*
	Plasma	*Interstitial fluid*	
Volume (litres)	3	9	30
Potassium	2% of total 3 g or 78 mEq (av. 5 mEq /litre)		98% of total 147 g. or 3,800 mEq. (av. 150 mEq./litre)
Sodium	60% of total 40 g or 1,800 mEq (av 145 mEq./litre)		40% of total 25 g or 1,100 mEq. (av. 36 mEq /litre)

This convenient arbitrary division of body water is unrealistic because there is continuous exchange of water and solutes between the component fluid divisions. The small volume of intravascular fluid circulates rapidly within the vessels and exchanges across the capillary wall with interstitial fluid. The interstitial fluid in turn circulates amongst the cells of the tissues, and transfers take place between interstitial and intracellular fluid across the cell membrane. The rate and extent of movement of water and of sodium, potassium, chloride and other elements readily soluble in water have been extensively studied by using radioactive isotopes and other materials as tracer substances Heavy water diffuses rapidly through the body fluids and cells, and reaches a new equilibrium both in cells and extracellular fluid within about two hours of its injection; this indicates a high degree of permeability to water in cell and capillary walls Radioactive sodium reaches a primary equilibrium about one hour after injection, apparently as the result of diffusion throughout the extracellular fluid; a secondary equilibrium is reached only after about 20 hours, probably as the result of passage of sodium into cells and bone. Potassium behaves differently from both sodium and water in that extracellular equilibrium is achieved more slowly, after about five hours, the rate at which equilibrium is achieved in the cells varies from tissue to tissue. There is rapid immediate uptake in the liver (McArdle and Merton, 1952) whereas equilibrium in the red cells may not be reached for more than 24 hours.

The difference in the rate at which sodium and potassium ions cross the cell boundary —and thus the relative concentrations of these two ions inside and outside the cells— depends primarily on certain properties of the ions themselves. Potassium is known to penetrate a cell boundary more rapidly than sodium, and this difference is probably exaggerated by the negative electrical charge on the cell membrane and may be further varied by transient local changes in *p*H. It seems quite certain that the former conception of the cell membrane as a rigid structure which could completely segregate sodium and potassium on opposite sides is wrong, if only for the reason that it offers

no explanation of how potassium reaches the interior of the cell. It is probably equally certain that there is a continuous ebb and flow of sodium and potassium across all cell membranes at varied rates, and that in some cells, such as those of the nervous system, function may depend largely on the electrical effects of such chemical transfer.

The total volume of the extracellular fluid depends on the body content of the cation sodium and its associated anions such as chloride. Because the capillary endothelium is freely permeable to these ions they do not play any part in the allocation of fluid between plasma and interstitial fluid. It is believed that the passage of fluid in both directions across the capillary endothelium depends on two pairs of factors: (1) the hydrostatic pressure of the plasma and the colloid osmotic pressure of the interstitial fluid move water and solutes into the interstitial fluid from the plasma; and (2) the hydrostatic pressure of the interstitial fluid and the colloid osmotic pressure of the plasma move water from interstitial fluid into the plasma. This general hypothesis depends on the supposition that the capillary endothelium is permeable to water and ions such as sodium, chloride and potassium, but is impermeable to the plasma albumin and globulin. Although the hypothesis is probably broadly true for peripheral capillaries, even in these wide variation is known to occur. In some circumstances there is outflow of fluid and solutes from the arteriolar end of the capillary and inflow from the tissues at the venous end; in other circumstances there is outflow from the whole length of a capillary, and return may be into another capillary or through lymphatic channels The low hydrostatic pressure in the portal vein capillaries [illegible] During

swelling due to excess interstitial fluid. Local change in extracellular fluid thus depends on change in capillary permeability.

The normal volume relationship of 1 : 3 between plasma and interstitial fluid is maintained in spite of a daily transfer of 1,100 litres of fluid from plasma to interstitial fluid, and their return to capillaries or as lymph.

Renal regulation of electrolyte and water

Sodium

In the normal subject the kidneys, by their control of the body content of sodium, *afford the most important means of regulating extracellular fluid volume* and, indirectly, total body water The renal functional efficiency is shown by the ability to reabsorb 99 per cent of the sodium, chloride and water of the 180 litres of fluid, containing over a kilogram of sodium chloride, filtered from the 1,100 litres of plasma flowing through the kidneys each day. About 85 *per cent of the filtered sodium* is actively reabsorbed in the proximal convoluted tubules and the remainder in the distal convoluted tubules, at least partly under the influence of adrenal cortical hormones. The degree to which sodium is reabsorbed depends also on the plasma sodium concentration, because when this tends to fall on account of sodium loss, tubular reabsorption is more complete. During starvation, excretion of sodium rapidly declines and reaches a minimum which is maintained until intake is resumed. As will be described later, sodium reabsorption is increased after injury and during inflammation, possibly also through the influence of adrenal cortical hormone. Retention of sodium also occurs in cardiac failure.

Potassium

The renal control of the body content of potassium is fundamentally different from that of sodium. There is no satisfactory evidence that potassium can be conserved by the kidney, and much more cause to believe that it would be biologically unsound for

this to occur. Although potassium is absorbed like sodium in the proximal tubules, it seems likely that it can be actively secreted by the distal tubules because more may be found in the urine than could be accounted for by the glomerular filtrate. If the extracellular concentration of potassium is not to rise to toxic levels during the tissue catabolism of starvation and after injury, the urinary excretion of potassium derived from the catabolized cells must be maintained During restriction of water intake and loss of body secretions, part at least of the water requirements of the body are derived from intracellular fluid, and this is possible only if potassium can be got rid of by excretion in the urine. During starvation, renal inability to conserve potassium results in a continued daily loss of potassium in the urine of about two to three grammes. The slow decline in the daily loss of potassium as a fast progresses is probably an expression of the law of mass action; as the total body potassium (or protein) decreases, so does the daily loss. When the urinary excretion of potassium decreases as in extreme oliguria or anuria, the extracellular concentration of potassium rises; in anuria a common mode of death is cardiac arrest due to potassium accumulation in the extracellular fluid. The maintenance of a normal extracellular potassium concentration is an important condition for normal function of the cells, and it is remarkable how this is achieved even when total intracellular potassium is grossly depleted. Excessive administration of potassium salts is countered by excretion of the excess potassium in the urine, provided urinary volume is sufficiently large

Water

About 85 per cent of the water filtered by the glomerulus is absorbed along with sodium and other ions in the proximal convoluted tubule. The remainder is reabsorbed in the distal tubule, with the exception of about one per cent of the original filtrate which forms the urine. The final volume of the urine depends largely on the total quantity of solutes requiring excretion by the kidney, because there is a minimal volume of water in which these solutes can be dissolved. The daily quantity of solutes requiring excretion varies with the food intake and with the metabolic state of the patient. Normal urine is hypertonic in relation to plasma, and the concentrating capacity of the kidneys also governs the minimum volume of water in which the solutes requiring removal can be excreted. Water ingested in excess of the requirements for insensible loss, sweat formation and minimal urine volume is excreted as additional urine

Extrarenal water losses

Insensible water loss

Dubois (1927) estimated that the average insensible loss of water as water vapour by diffusion through the skin and in the expired air was 0·5 gramme of water per kilogram of body-weight per hour, or 840 millilitres per day for a 70-kilogram patient. Gamble (1946–47) obtained a similar figure by direct weighing in normal subjects. Insensible water loss is inevitable, and because of the important part it plays in metabolic heat loss, it is essential for survival. It must be considered as the primary water requirement of the body, because it will continue, and must be satisfied regardless of other needs and abnormal fluid losses

Faeces

The volume of water lost in the faeces depends on the residue of the food, and in fasting is very small. On a normal diet, up to 200 millilitres per day should be allowed for loss in the faeces, which makes the total extrarenal loss of water up to 1,000 millilitres per day. The daily obligatory water expenditure thus consists of the total extrarenal loss together with the minimal volume of water required for urine formation of at least 500 millilitres, making 1,500 millilitres in all.

Metabolism in fasting

Deprivation of water and food

When a normal adult is deprived of both water and food, about 200 millilitres of water are derived from the oxidation of fat and protein, but the remaining 1,300 millilitres of the minimum water requirement must be obtained from the body water. Gamble (1946–47) found that this volume of water is obtained from both extracellular and intracellular compartments, and that there is an accompanying loss of sodium and potassium from the body. In dogs, the loss of sodium is greatest on the first day and thereafter declines and is very small after the fifth day, whereas there is a steady loss of potassium throughout the fast. This mobilization of intracellular fluid thus allows of the provision of water and enables the volume of extracellular fluid to be maintained by renal conservation of sodium. Dehydration by thirsting leads to death when about 40 per cent of total body water has been lost, equivalent to 17 litres in a 70-kilogram man which, at 1,300 millilitres per day, will be lost in about 13 days.

Deprivation of food, water being supplied

When ample water is provided for a fasting subject, oxidation of body fat and protein for the provision of calories continues with the production of about 200 millilitres water of oxidation and, following the cellular catabolism, the liberation of a small quantity of intracellular water and potassium. Intracellular water no longer need be made available for basal water needs, and renal conservation of sodium prevents more than slight loss of extracellular fluid. Because it was freely available, Gamble's subjects usually drank more water than their basal requirements, and excreted about 800 millilitres of urine per day which he therefore considered to be the minimum urine volume for fasting subjects under basal conditions; this figure agrees closely with the present writer's observations on surgical patients under similar conditions before operation.

Deprivation of food, water and glucose being supplied

When otherwise fasting subjects ingest 100 grammes of glucose each day, ketosis is prevented and catabolism of protein tissue is reduced, the solutes requiring removal in the urine are reduced by about 50 per cent, and the daily minimum water requirement for urine formation also is halved. The provision of more than 100 grammes of glucose per day will not reduce protein catabolism any further, because this quantity of glucose lowers protein breakdown to about 40 grammes per day, which is the minimum rate for protein metabolism. Administration of glucose also reduces the loss of sodium during fasting but increases equivalently the loss of potassium. The daily administration of 2 litres of a 5 per cent glucose solution provides 100 grammes of glucose and a large surplus of water.

Effects of surgical and accidental injury

Shrinkage of the tissues and loss of body-weight have long been recognized as inevitable sequelae to accidental or surgical injury, inflammations, fevers and other acute illnesses. Often the loss of weight has been largely ascribed to loss of body fluids by diarrhoea or vomiting or to consumption of tissue by starvation. The work [illegible] been followed [illegible] and it is now clearly recognized that the well-nourished human body [illegible] a characteristic way to injury. Certain features of this response have an important influence on treatment after operations.

During the first two weeks after a major operation there may be a loss of weight amounting to from 5 to 10 per cent of the initial weight. During the first 48 hours,

even in the absence of infection, body temperature, pulse and respiration rates are increased, a reaction recognized since ancient times and formerly called the "traumatic fever". The changes in urinary volume and constituents following gastrectomy in a well-nourished male patient are shown in Fig. 65 on page 130, and are fairly typical for other kinds of severe injury.

During the first week after injury there is an increase in nitrogen excretion, a shorter increase in potassium excretion and a reduction in sodium and chloride excretion and in urine volume. There may also be an increase in extracellular fluid volume, chiefly affecting the interstitial fluid. In the second week, water, sodium and chloride are excreted in larger quantities than before operation, whereas nitrogen excretion falls towards the pre-operative quantities. By about the end of the second week these changes all tend to pass off and metabolism seems to return to normal. Simultaneous changes in the urinary output of products of steroid metabolism suggest the participation of the adrenal cortical hormones in these metabolic disturbances, and this is supported by the marked reduction in the number of circulating eosinophils on the day of injury or operation

These metabolic changes follow injury to all well-nourished patients and persist in spite of all attempts to modify them. This seems to indicate that they are part of a normal reaction to injury. They are not due to starvation, although poor nutrition modifies considerably the output of nitrogen after injury. The increase in nitrogen excretion is due to catabolism of body protein, and this occurs although a full quota of calories is supplied; it cannot be prevented by providing protein, either whole or hydrolysed, by mouth or by intravenous infusion, even when accompanied by adequate non-protein calories. Although during the first week the protein catabolism cannot be reduced by supplying calories, after the first week tissue destruction can be prolonged and increased by restriction of food intake and especially of calories. The retention of water, sodium and chloride by the kidney occurs almost regardless of the quantities of these given or the route of their administration, and is related in time to the increase in the volume of the extracellular fluid and to the formation of the inflammatory exudate in the injured tissues. The diuresis of water, sodium and chloride in the second week is similarly related to the resolution of that exudate. Potassium is not retained in this way by the kidney, and for a short time after injury potassium is excreted in high concentration in the urine and in such a large quantity that it must have come from the cells, because it exceeds in quantity all the potassium of the extracellular fluid. This large potassium diuresis occurs too soon to be the result of tissue breakdown. An alternative explanation is that it is due to the transfer of potassium and its associated water out of cells, the potassium being then excreted in a more concentrated solution by the kidneys. In this way some intracellular water is freed of its potassium and is made available for insensible loss. In animals, Fox and Baer (1947) found a large movement of sodium, water and chloride from uninjured to injured tissues with an increase in the quantity of these ions in the injured and inflamed area. There was a simultaneous large shift of potassium and water away from the uninjured region, and a loss of potassium from the body. This affords additional evidence of the shift of body fluid following injury which Cameron (1946–47) described as occurring after injury with vesicant gases and similar agents.

CLINICAL DISTURBANCES OF BODY FLUIDS

Disturbances of sodium

In the normal subject at least 60 per cent of the total sodium is in the extracellular fluid, about 30 per cent is more or less fixed in bone and is only slowly available, the remaining 10 per cent being in the intracellular fluid.

The quantities of sodium and chloride excreted in the urine vary with the intake and loss by other routes, the chief losses of this kind being by vomiting or diarrhoea and by excessive sweating due to either occupational or climatic factors. There is some evidence that the wide variations in the sodium content of sweat are related to the total body content, and that the concentration of sodium in both sweat and urine falls when output exceeds intake. Except during the first week after injury and during inflammation due to other causes—when sodium intake is greater than the extrarenal losses—the excess is excreted in the urine. Because of the conservation of sodium by the kidneys and sweat glands which follows partial depletion of the body sodium, no absolute value for daily output and, hence, for intake of sodium can be laid down, but an average quantity for temperate climates is 5–6 grammes per day of sodium chloride (80–100 mEq. sodium), less than 10 mEq. sodium are lost in formed faeces, negligible quantities in sweat and 70–90 mEq. (4·5–5·5 grammes as sodium chloride) in the urine. For extra losses in sweat, a variable quantity of salt should be added according to the temperature and humidity and to the amount of work to be done. It is fairly certain that under temperate conditions an intake of 10–15 grammes per day is usually excessive and is unnecessary; when administered as isotonic saline during the first week after injury, such quantities lead to a large increase in extracellular fluid volume and may cause oedema. To limit loss of sodium by sweating, especially in young children and babies, overheating of patients should be avoided during operation; the use of rubber sheeting should be restricted, and the temperature of the operating theatre should not exceed 80° F. In hot climates, if an air-conditioned theatre is not available, operations should be performed in the early morning.

Large volumes of intestinal secretions are rapidly lost in acute obstruction high in the small intestine. The lost secretions are initially derived from the blood plasma which in turn is replenished from the interstitial fluid. The detailed composition of the fluids which may be lost are shown in Table III, but in acute losses of large volumes of secretions the main disturbance is a large reduction in water and sodium, a depletion of extracellular fluid volume. The most severe example of this type of loss is seen in Asiatic cholera, but very rapid reduction of extracellular fluid volume also occurs in acute obstruction of the small intestine, ulcerative colitis and in diarrhoea from an ileostomy.

TABLE III

COMPOSITION OF INTESTINAL SECRETIONS

Secretion	Concentration in mEq. per litre				Volume per day (ml)
	Na^+	K^+	Cl^-	HCO_3^-	
Gastric	50	10	150	—	2,500
Intestinal	140	10	100	25	3,000
Biliary	140	5	100	30	500
Pancreatic	140	5	70	70	700
Cf plasma	145	5	105	27	—

Clinical features of sodium deficiency

The fluid loss causes an increase in the plasma-protein concentration, packed cell volume and blood viscosity, and may thus mask pre-existing reduction of the plasma-protein concentration or anaemia. There may be a marked reduction in circulating blood volume with compensatory vasoconstriction, low systolic and diastolic blood

pressure, fast pulse rate and small constricted veins containing sluggishly flowing dark blood. The tongue is dry and hard, the eyes are sunken, the skin is dry and wrinkled and the subcutaneous tissues are lax. The urine is scanty, dark in colour and of high specific gravity. This is the state frequently called "dehydration", but the most important feature is the loss of base (sodium) and of water. Plasma-sodium concentration may not be altered by the loss of intestinal secretions, and the deficit of sodium may become evident only when the lost fluids are replaced with solutions containing inadequate quantities of sodium. Because there may be accompanying losses of potassium and chloride or of bicarbonate, it is essential to determine at the same time the plasma concentrations of sodium, potassium, chloride and bicarbonate; measurement of packed cell volume will indicate the degree of concentration or dilution of the blood

The extracellular concentration of sodium may be lowered without change in the total quantity of sodium by the rapid intravenous infusion of fluids which do not contain sodium, especially when diuresis is delayed or reduced after injury. The shift of sodium into the cells in potassium deficiency may be due partly to the increased quantity of extracellular sodium following saline infusions, and partly to the electro-chemical deficiency which may result from potassium loss from the cell.

Extracellular sodium concentration, as well as the total quantity of sodium, may be increased by the injection of hypertonic saline (2–10 per cent), and temporarily and to a limited degree during the diuresis which follows the injection of hypertonic glucose solutions. Except in water intoxication (*see* page 106), the administration of hypertonic saline is not advisable in the correction of sodium deficits because of the serious disturbances of cardiac function which may result from a too rapid intravenous injection of strong saline.

Disturbances of potassium

Each day the healthy adult consumes about 2 or 3 grammes (52–78 mEq.) of potassium in food, 2–5 grammes (52–130 mEq.) are secreted into and reabsorbed from the alimentary tract, 2–3 grammes (52–78 mEq.) are excreted in the urine and a very small quantity in the faeces and sweat. Only about 2 per cent (80 mEq.) of the total body content of potassium is in the extracellular fluid and 98 per cent is in the cells, about 80 per cent of which is in the skeletal muscles. Because the kidneys are unable to conserve potassium as they do sodium, the daily excretion of up to 2 or 3 grammes (52–78 mEq.) of potassium in the urine continues at all times. In the tissue breakdown of starvation, 10–12 milligrams (2·5–3·0 mEq.) of potassium are lost for every gramme of nitrogen, but this is a balanced loss at a fairly steady daily rate. Because of this continuing loss of potassium in the urine, the body content of potassium falls when intake is reduced or stopped by starvation, by restriction of diet, by vomiting, or when the output is increased by loss of intestinal secretions. Potassium excretion in the urine is increased by the administration of ACTH, cortisone, desoxycorticosterone and by infusions of solutions containing sodium salts and glucose.

Potassium deficiency

It will be seen from Table III that the concentration of potassium in the gastro-intestinal secretions may be up to twice that in the plasma, whereas the concentrations of sodium and chloride seldom exceed, and are often less, than their concentration in plasma. In acute losses of gastro-intestinal secretions, the lost fluid resembles more or less closely, and is derived from, the extracellular fluid, but contains more potassium than this fluid; this potassium loss is relayed through interstitial fluid to intracellular fluid. Nevertheless, in acute losses of short duration, only about 4 per cent of total body potassium but up to 25 per cent of total available body sodium may be lost

(Darrow, 1945). In treatment, the immediate emphasis is rightly on the correctic sodium and water loss by the intravenous infusion of isotonic saline, that is, o placement of extracellular fluid. The repetition of such losses of intestinal fluids, the replacement of sodium but not of potassium, eventually leads to the loss of 25 per cent of the original content of potassium. In addition to the potassium l in the intestinal fluids there are small losses associated with the saline infusi Unlike the steady daily loss in starvation, which is proportional to the loss of nitro the quantity of potassium lost in intestinal secretions varies with the volume o vomitus or fistula drainage, and with the level of origin of the secretions.

Clinical features of potassium deficiency

Because the daily loss of potassium is small, there is in most cases of severe po sium deficiency a long history of loss of secretions. The clinical picture varies gre but the most striking feature of severe deficiency is intense drowsiness or even co the onset of which is gradual. The patient lies slumped in the bed, the head droo down on one shoulder and the jaw hanging slackly; roused with difficulty, he o his eyes slowly and with obvious effort, blinking and screwing up his face, and apparently too tired to go on looking, his eyelids fall and he once again beco drowsy. Speech is slow and indistinct, he is liable to break off in the middle sentence or quickly lose his temper; such patients are often easily irritated and s much change in personality. After recovery it is common to find amnesia for period of the most severe disturbance.

There seems to be muscular weakness as well as apathy, and perhaps neuromusc incoordination, there may be loss of deep reflexes, difficulty in swallowing inhalation of food or drinks, and incontinence of urine is common, perhaps beca the sensation of fullness of the bladder is impaired.

A chronic ileus and abdominal distension are common features of post-opera potassium deficiency and are due to diminished intestinal motility and to loss muscle tonus. Apart from the accumulation of secretions in pyloric stenosis, whic associated with oedema as well as with hypertrophy of the gastric wall, ileus does seem to be common before operation. Severe pain coinciding with visible gas peristalsis is fairly common in advanced pyloric stenosis but, especially when as ciated with latent tetany, this may be due to a relative deficiency of calcium relate the alkalosis.

The very drowsy or comatose patient may exhibit phasic respiration when ther severe alkalosis, or air hunger when there is associated acidosis.

The serum-potassium concentration is usually but not always reduced, becaus depends on extracellular fluid volume and urinary output and on the rate of mobili tion of intracellular potassium as well as on the total body content. In deficiency limits of normal serum-potassium concentration are 16–25 milligrams per 100 mi litres (4·1–6·4 mEq. per litre); a raised concentration is more dangerous than a l one. The peripheral blood pressure is lowered, the pulse rate is slow but the superfic veins are well filled, the skin is warm and there may be a reddish-purple flush cyanosis of the face and on the back of the hands. The heart is usually enlarged a changes in the electrocardiographic tracing are often found but vary widely, are n always present even in very severe deficiency and are not closely related either to severity of the disturbance or to the serum-potassium concentration. The followi alterations may be found. increased QT interval, decreased height and inversion [illegible] and prolongation of T-wave, depression of ST or inversion of P-wa [illegible] When they are due to potassium deficiency, improvement is usually [illegible] administration of potassium salts.

Diagnosis of potassium deficiency

Potassium deficiency should be suspected whenever there has been prolonged loss of gastro-intestinal secretions or severe restriction of food intake, and when there is severe alkalosis or acidosis. It is predisposed to by the intravenous administration of fluids which do not contain potassium, especially when such therapy is the sole source of fluid and calories Diagnosis is most surely made by the clinical appearance of the patient, the finding of a low serum-potassium concentration, or typical electrocardiographic abnormalities are valuable supporting evidence, but are often absent and are seldom the only signs of deficiency. It is important to remember that significant decreases in serum-potassium concentration may be found in the absence of characteristic signs and symptoms of deficiency, and that not all cases of severe deficiency are associated with depression of the serum-potassium concentration. In slowly advancing deficiency, the serum-potassium concentration usually falls only when the total loss is very large, on the other hand, the very rapid loss of intestinal secretions containing two or three times as much potassium as extracellular fluid may cause acute depression of serum-potassium concentration, which is rapidly restored from the cells when the fluid loss stops, especially if there is oliguria

Treatment of potassium deficiency

Replacement of a large deficiency of potassium (23 per cent of initial body content, 1,000 mEq or 40 grammes) takes several days and requires large quantities of potassium salts, because some of the administered potassium is excreted in the urine. When the patient is comatose, the intravenous administration of as little as one gramme of potassium chloride may lead to the rapid recovery of consciousness, there is a similar rapid improvement in the mental state of irritable and drowsy patients. Unless there is an adequate output of urine, intravenous infusion of potassium salts may raise extracellular potassium concentration to a toxic level (above 27 milligrams per 100 millilitres, or 7 mEq. per litre), and result in cardiac arrest Before starting the intravenous infusion, it is therefore wise first to ensure that urinary output exceeds 500 millilitres in the 24 hours (or 20 millilitres per hour), if necessary by the prior administration of a 5 per cent glucose solution, and to replace most of the deficit by oral administration. With potassium deficiency there is severe alkalosis when the disturbance is due to vomiting of gastric secretions, or acidosis when it is due to diarrhoea. In alkalosis, potassium chloride should be employed and, provided urinary volume is adequate, up to 2 grammes (containing 26 mEq. potassium) may be administered over a period of 4 hours by the intravenous route. Depending on urinary volume and the clinical state of the patient, a further 2 grammes of potassium chloride may be given preceded by 500–1,000 millilitres of 5 per cent glucose solution if urinary volume is inadequate. Up to 12 grammes of potassium chloride per day (containing 156 mEq. potassium in doses of 2 grammes every 4 hours may be administered orally to co-operative patients whose daily output of urine exceeds 500 millilitres. When there is associated acidosis, this is corrected by the intravenous administration of sodium lactate with the potassium chloride (in Darrow's solution), and subsequently, potassium citrate is given by mouth in 2-gramme doses every 4 hours. Because of nausea and anorexia, it is often necessary to start replacement by intravenous infusion, even when the patient is able to drink. The remission of symptoms after potassium replacement is not conclusive proof that they were due solely to potassium deficiency, because restoration of potassium has effects on the other abnormalities associated with potassium deficiency, such as alkalosis. The only certain way to judge when a large intracellular deficit of potassium has been replaced is by carrying out a potassium balance study during the period of replacement. This means comparing the daily output of potassium in the urine with the intake; when potassium is being *retained*, intake exceeds output, but when replenishment is complete, urinary output increases

until it closely approaches the intake. Unless the deficit is corrected before operation, the post-operative starvation and the large urinary excretion of potassium immediately after operation may together cause an acute disturbance.

During convalescence from operations, severe injuries and other extensive inflammations, it is theoretically advantageous to increase the daily intake of potassium, especially when less than a full diet is being consumed. Good natural sources of potassium in a palatable form are such well-recognized "invalid foods" as chicken or beef tea, broth, meat extracts, fruits and fruit juices. The addition of dried milk powder to soups, sauces and custards also increases the potassium intake, and black treacle is a very rich source.

Potassium retention

Elevation of the serum-potassium concentration is usually associated with extreme oliguria or anuria, it is due to the incomplete excretion of potassium derived from the cells which therefore accumulates in the extracellular fluid. It may also be due to excessive intravenous administration of potassium salts when urinary volume is low, but seems to be very rare after oral administration or when the precautions for intravenous administration previously stressed are observed. In most reported cases the serum-sodium concentration has been low, and the resulting alteration of sodium-potassium equilibrium may further explain the clinical disturbance.

Clinical features and diagnosis of potassium retention

Associated with a high serum-potassium concentration there is mental confusion and apathy with weakness of the limbs and sensory disturbances. The peripheral circulation is poor, the skin is cold, pale, greyish and cyanosed, the blood pressure is low, the heart rate is slow and may be irregular and cardiac arrest may follow. Electrocardiographic changes are more common with high than with low serum-potassium concentrations, and may appear when the serum potassium reaches 27 milligrams per 100 millilitres (7 mEq. per litre) and are always present at concentrations of 30 milligrams per 100 millilitres (8 mEq. per litre) The T-wave is peaked, and the duration of the QRS complex and the P-R interval are increased.

Treatment of potassium retention

Whether treatment can be successful depends on the cause of the disturbance. When it is due to excessive intravenous administration, the flow of fluid containing potassium must be stopped and a 5 per cent glucose solution should be rapidly injected. If associated with water intoxication or sodium depletion, the administration of hypertonic sodium chloride solution is required to restore urinary function. When there is anuria the necessity to limit water and sodium intake seriously restricts the therapeutic possibilities. If a fat emulsion is being supplied by an intragastric drip, the best possibility would seem to be the use of a suitable ion exchange resin, although the value of this is limited because of the interference with the administration of the fat emulsion (*see* page 123).

Alkalosis and acidosis

Regulation of the *p*H of the blood within narrow limits is essential for normal function of the body. A [illegible] blood *p*H largely depends on the ratio of [illegible] of The concentration of ca[illegible] bicarbonate *on the total quantity of* base (cation) available to form bicarbonate. "Total available base" is indicated by the amount by which the sum of the cations in the plasma (sodium, potassium, calcium and magnesium) exceeds that of anions

(chloride, phosphate, sulphate, the keto acids and protein). In most surgical conditions it is necessary to consider only sodium, potassium, chloride and bicarbonate (Table IV).

TABLE IV

NORMAL COMPOSITION OF PLASMA
(Modified from Gamble, 1946–47)

"Base" or Cations⁺ (mEq/litre)		*"Acid" or Anions⁻ (mEq/litre)*	
Na^+	142	Cl^-	103
K^+	5	HCO_3^-	27
Ca^{++}	5	HPO_4^{--}	2
Mg^{++}	3	SO_4^{--}	1
		Organic acids	6
		Protein	16
	155		155

Much confusion has resulted from the varied use made of the terms alkalosis and acidosis. This may be avoided if the term alkalosis is confined to the state in which alkali reserve or plasma bicarbonate is increased, and if acidosis is confined to the state in which there is decrease in plasma bicarbonate or alkali reserve. Alterations in *p*H of the blood are best indicated by the terms acidaemia and alkalaemia. The "gaseous" type of alkalosis due to forced breathing and gaseous acidosis due to depression of respiration are not common in surgical patients.

Alkalosis

Alkalosis most commonly results from a deficit of chloride due to loss by vomiting or by gastric aspiration, the lost chloride being replaced by bicarbonate. Both sodium and potassium also are lost in smaller quantities than chloride in the vomitus or aspirated fluid. When food intake is impaired over a prolonged period, the continuing daily loss of potassium in the urine may result in a large deficit of potassium Because of efficient renal conservation of sodium the relative excess of sodium is maintained, and in the later stages there is a transfer of sodium into the cells to replace the potassium which has left them. The resulting increase of intracellular sodium concentration disturbs the normal sodium-potassium equilibrium inside the cell and across the cell membrane between intracellular and extracellular fluids. Cooke and his associates (1952) have estimated that up to 50 per cent of the intracellular potassium may be replaced, two-thirds by an equivalent amount of sodium, the remaining third by hydrogen ion.

These changes in the composition of the cells which accompany alkalosis due to prolonged vomiting or to gastric aspiration can be corrected only by displacing sodium and hydrogen ions from the interior of the cells by administering potassium salts This effect of the administration of potassium results in improvement in clinical state, even although insufficient chloride is administered to correct the alkalosis. The administration of sodium chloride will increase the transfer of sodium into the cells, and is accompanied by an increased urinary loss of potassium. The relative excess of sodium is not then diminished unless sodium is preferentially excreted, so that alkalosis will persist. Because the shift of sodium into the cells reduces the quantity of sodium available for combination with bicarbonate in the extracellular fluid, this transfer may be regarded as an additional buffering system for the excess of alkali. Unfortunately, the sodium transferred to the cells is undetectable by ordinary methods

of investigation, and no idea of its extent is given by determinations of extracellular or plasma-sodium concentration.

Alkalosis with potassium deficiency is also a feature in certain forms of Cushing's syndrome and in some types of adrenal cortical neoplasms. In these cases the potassium deficiency is probably the primary disturbance, being due to the increased excretion of potassium by the kidney induced by steroid hormones produced by the tumours. A similar effect may be produced by prolonged administration of desoxycorticosterone acetate.

Clinical features of alkalosis

The most obvious clinical feature of alkalosis is usually the phasic respiration; after a period of apnoea, which varies in duration according to the severity of the alkalosis from 5 to 30 seconds or more, respiration begins at first shallowly and then with increasing depth until, after one or two normal breaths, the range of the respiratory excursion declines once more. The number of breaths in each cycle varies from 5 or 6 to 10 or more, and with the variation in depth seems also to be related to the severity of the alkalosis. Latent tetany is also found in severe alkalosis, probably because of depression of the serum-calcium concentration (*see British Surgical Practice*, Vol 8, p. 200). There is also elevation of the serum bicarbonate to 80–120 volumes per cent (36–54 mEq. per litre) and the urine is acid in reaction (pH 5·0). This association of an acid urine with alkalosis is well known, and as long ago as 1924 was produced experimentally in dogs by Gamble and Ross. It is most commonly found following large losses of gastric juice when sodium depletion leads to renal conservation and to the reduction of the sodium concentration in the urine. The urine becomes and will remains acid until sodium reappears in it. As Gamble (1922) showed, urine always contain as much free carbonic acid as does the blood, and in the absence of sodium from the urine this is excreted as free acid and the urinary pH falls to about 5·0.

Treatment of alkalosis

The deficit of chloride should be replaced together with the smaller deficits of base. As has been indicated, with severe alkalosis there is usually also a large deficit of [illegible] with a cation which can be converted to urea and excreted, should be avoided when there is potassium deficiency.

Acidosis

Acidosis may be due to reduction in the quantity of base available to form bicarbonate or to increase in the fixed acids. A relative increase in acid may be due to the production of keto acids in starvation or in diabetes, or to the retention of acid in renal insufficiency. Relative reduction in base most often results from the loss of sodium in small intestinal or biliary secretions, and may also occur after losses of large and lower small intestinal secretions in diarrhoea from any cause, in ulcerative colitis and after transplantation of both ureters. There are usually accompanying deficits of water, potassium and chloride, but probably only when the potassium deficit [illegible] loss.

As in alkalosis, the most obvious clinical feature in severe acidosis is a change in

respiration which becomes rapid, deep and raucous, the classical picture of air hunger. The respiratory rate may increase to as much as 50 per minute or more, but there are intervals during which the patient tries to moisten his lips with his tongue, usually without success because the tongue is dry, brown and hard. The pulse rate is increased and both systolic and diastolic blood pressures are raised.

Treatment of acidosis

The low serum bicarbonate can be corrected by the provision of base as sodium or potassium with lactate or citrate to increase the bicarbonate concentration. When the base deficiency is due to sodium loss, saline lactate solution should be used. In losses of small intestinal fluid in diarrhoea Darrow's solution, which contains potassium, should be used. Severe acidosis should not be completely corrected by intravenous infusions; potassium or sodium citrate should be given orally as soon as drinking can be tolerated.

Thirst

The sensation of thirst is not well understood. It may be due primarily to local dryness or other changes in the pharynx, or to change in the concentration of body fluids, or to both types of factor. It is evident from animal experiments that water is roughly measured in the pharynx as it is drunk. The urge to drink to satisfy a water lack can be abolished temporarily by sham-drinking, through contact in the throat, or more lastingly by placing water in the stomach through a tube. Adolph (1947) found that in thirsty subjects water deficits were proportional to the amount subsequently consumed in slaking their thirst, or to the urge to drink. During the first 24 or 48 hours after injury, thirst can be relieved for short periods of time only, 15–30 minutes, by the consumption of water, tea or other fluids, and is not diminished by the intravenous infusion of isotonic saline or glucose solution. It seems possible that during the period after injury when potassium is leaving the cells to be excreted in the urine, thirst is chiefly due to intracellular dehydration, transient relief is afforded by wetting the pharynx, even although the swallowed fluid is vomited and little of it is absorbed into the blood stream. It would seem better to give mouth washes rather than drinks, and in practice this appears to be effective.

When, following operations on the alimentary tract, the patient is allowed to drink unlimited quantities of fluid but distension of the stomach is prevented by aspiration, thirst often increases. There is a disproportionately larger increase in the aspirations as the intake increases, and this becomes the cause of very large losses of base and of chloride as well as of body water.

Dehydration

This term is widely but loosely used to indicate reduction in the body content of water when the output of water exceeds the intake, without reference to the loss of base which usually accompanies loss of body water. Because body water is intimately associated as water of hydration with the ionic constituents of the body fluids, if water alone is lost there will be an increase in the concentration of these constituents. To counteract the development of such a hypertonic state, base is excreted by the kidneys. True dehydration in the restricted sense of loss of water alone is rare, but in the wider sense in which the term is usually employed, a variety of causes and combinations of base and of acid loss may be encountered.

Restriction of water intake

Water loss as vapour in the expired air and through the skin continues unabated, although the volume of sweat and urine is greatly reduced. The rate of insensible

water loss is increased by fever and high environmental temperature. The body water which is expended in this way is derived both from extracellular and from intracellular fluid. If the loss of water is not speedily replaced by drinking, base is excreted in the urine.

Loss of water by vomiting, diarrhoea, excessive urine formation or sweating

In each of these kinds of loss there is associated loss of base, either directly as in vomiting and diarrhoea, or secondarily in polyuria and when sweating is copious or prolonged.

Unless the lost base is replaced, water cannot be retained even when it is provided in adequate quantity. Replacement of base must be qualitative as well as quantitative if the replaced water is to reach its proper destination. In a temperate climate, total fluid output is up to 2–3 litres per day, about 50 per cent being urine. In a hot dry climate up to 11 litres per day may be lost, 90 per cent of which is sweat. A limited water debt can be incurred, mostly of intracellular water. A loss of 5–10 per cent of the total body water is easily and rapidly corrected by the consumption of water and food; so rapidly is it improved by drinking water that is seems likely that loss of base lags behind loss of water, and provided the water debt is not too prolonged, much of the associated base will still be in the body.

Oedema

Oedema is an excessive accumulation of fluid in the tissue spaces and is due to disturbance of the mechanisms of fluid interchange. It is often difficult to explain the occurrence of widespread oedema in surgical patients. Low concentration of the plasma proteins, especially of albumin, should always be considered; this may be the result of malnutrition, either before or after operation, or of protein depletion by prolonged losses of exudate from extensive granulating surfaces in burns or large abscess cavities. The reduction in concentration may also be due to dilution following an increase in extracellular fluid volume. This is most likely to be caused by the intravenous infusion of excessive volumes of glucose solution or of saline during the immediate postoperative period when renal excretion, even of water, is much slower than in the normal person.

On clinical examination of the patient, excessive accumulation of extracellular fluid is not always readily recognizable as oedema. Large quantities of fluid may accumulate before there is pitting on pressure, even in the dependent parts such as the sacral region, the scrotum or the dorsum of the foot. Crepitations in the basal regions of the lungs are more commonly due to accumulation of bronchial secretion than to hydrostatic oedema of the lungs.

Water intoxication

Because of the danger of sodium retention during the immediate post-operative period, there has been a growing tendency to administer a 5 per cent glucose solution instead of isotonic saline. Even this is not without danger when large volumes are injected rapidly, because the delayed excretion of the water leads to retention of a large proportion of the administered fluid, and may give rise to the state of water intoxication. The effect of rapid dilution of the extracellular fluid by the addition of water is to lower the extracellular concentration of sodium. This leads to disturbance of the cation equilibrium at the cell membrane and is thought to result in the transference of water into the cells with consequent distortion of their function.

The rate of injection of glucose solution seems to be the most important factor in the production of water intoxication, combined with inability of the kidneys to respond by a rapid diuresis and with the consequent rapid dilution of extracellular

sodium. The concentration of sodium may be lowered slowly in chronic disturbances to an even greater degree than is found in water intoxication, without obvious ill-effects. The occasional danger of "pushing fluids" has long been emphasized (de Takats, 1931), and water intoxication has been described after rectal administration of water and after excessive drinking during the immediate post-operative period. A similar disturbance may arise when sodium depletion by vomiting or diarrhoea is exaggerated by replacement with sodium-free fluid such as glucose solution, or when vomiting patients are allowed to drink too freely (salt depletion syndrome (Peters, 1948)); in cardiac disease it is associated with a low salt diet, the use of mercurial diuretics or an excessive fluid intake (low salt syndrome (Schroeder, 1949)).

Clinical features

In the early stages of water intoxication there may be nausea and vomiting or diarrhoea, respiration is rapid and stertorous, there may be mental confusion and irritability, twitching of the limbs, epileptiform seizures and coma which may last for an hour or two, or for many days. After recovery there is usually amnesia. At first there is a diuresis, a large volume of very dilute urine being passed, but this is followed by oliguria or even anuria. Oedema is not common, but is usually most noticeable in the eyelids. At first the blood pressure is raised but later may fall; the haemoglobin and plasma-protein concentrations and packed cell volume are markedly lowered. Spontaneous recovery may follow the restriction of water intake. In 16 of the 17 cases reported by Zimmermann and Wangensteen (1952), the onset was within 48 hours of operation, and in 3 cases less than 3 litres of fluid had been administered.

Treatment

During spontaneous recovery the waterlogged patient lies in an irritable confused state for a week or more The process of recovery may be accelerated by the intravenous injection of hypertonic saline (5 per cent). Only a small volume, for example 200 millilitres, should be administered slowly, and the injection should be stopped if symptoms are relieved and if urinary secretion is established before all the fluid has been given. Too rapid injection of hypertonic saline may cause sudden cardiac arrest or circulatory overloading In this condition hypertonic saline is believed to act by increasing the extracellular sodium concentration, thus withdrawing water from cells and restoring normal equilibrium and function.

The influence of renal disease on body-fluid equilibrium

Enough has been said to indicate the very important part the kidneys play in the maintenance of both the volume and composition of the body fluids. Even in severe or advanced renal disease there is usually sufficient functional capacity to prevent gross distortion of the body fluids. Because of impairment of concentrating power and loss of specificity in reabsorption and tubular secretion, this equilibrium may be achieved only at the cost of an increased water turnover and urine volume. In chronic nephritis reduction in glomerular filtration reduces excretion of sulphate and phosphate. The inability to conserve sodium by the formation and excretion of ammonium may result in a reduction of extracellular fluid volume such as to cause a fall in blood pressure and peripheral circulatory failure. The combination of acid retention and sodium loss may lead to severe acidosis Loss of potassium also may be marked in advanced renal disease and may give rise to symptoms and signs of potassium deficiency when urine volume is large. In oliguria or anuria, retention of potassium may raise its concentration in extracellular fluid so high as to cause cardiac arrest.

The patient with advanced renal disease may therefore be a poor operation risk; survival must depend largely on the way the kidneys can deal with the further burdens

water loss is increased by fever and high environmental temperature. The body water which is expended in this way is derived both from extracellular and from intracellular fluid. If the loss of water is not speedily replaced by drinking, base is excreted in the urine.

Loss of water by vomiting, diarrhoea, excessive urine formation or sweating

In each of these kinds of loss there is associated loss of base, either directly as in vomiting and diarrhoea, or secondarily in polyuria and when sweating is copious or prolonged.

Unless the lost base is replaced, water cannot be retained even when it is provided in adequate quantity. Replacement of base must be qualitative as well as quantitative if the replaced water is to reach its proper destination. In a temperate climate, total fluid output is up to 2–3 litres per day, about 50 per cent being urine. In a hot dry climate up to 11 litres per day may be lost, 90 per cent of which is sweat. A limited water debt can be incurred, mostly of intracellular water. A loss of 5–10 per cent of the total body water is easily and rapidly corrected by the consumption of water and food, so rapidly is it improved by drinking water that is seems likely that loss of base lags behind loss of water, and provided the water debt is not too prolonged, much of the associated base will still be in the body.

Oedema

Oedema is an excessive accumulation of fluid in the tissue spaces and is due to disturbance of the mechanisms of fluid interchange. It is often difficult to explain the occurrence of widespread oedema in surgical patients. Low concentration of the plasma proteins, especially of albumin, should always be considered; this may be the result of malnutrition, either before or after operation, or of protein depletion by prolonged losses of exudate from extensive granulating surfaces in burns or large abscess cavities. The reduction in concentration may also be due to dilution following an increase in extracellular fluid volume. This is most likely to be caused by the intravenous infusion of excessive volumes of glucose solution or of saline during the immediate post-operative period when renal excretion, even of water, is much slower than in the normal person

On clinical examination of the patient, excessive accumulation of extracellular fluid is not always readily recognizable as oedema. Large quantities of fluid may accumulate before there is pitting on pressure, even in the dependent parts such as the sacral region, the scrotum or the dorsum of the foot. Crepitations in the basal regions of the lungs are more commonly due to accumulation of bronchial secretion than to hydrostatic oedema of the lungs.

Water intoxication

Because of the danger of sodium retention during the immediate post-operative period, there has been a growing tendency to administer a 5 per cent glucose solution instead of isotonic saline. Even this is not without danger when large volumes are injected rapidly, because the delayed excretion of the water leads to retention of a large proportion of the administered fluid, and may give rise to the state of water intoxication. The effect of rapid dilution of the extracellular fluid by the addition of water is to lower the extracellular concentration of sodium. This leads to disturbance of the cation equilibrium at the cell membrane and is thought to result in the transference of water into the cells with consequent distortion of their function.

The rate of injection of glucose solution seems to be the most important factor in the production of water intoxication, combined with inability of the kidneys to respond by a rapid diuresis and with the consequent rapid dilution of extracellular

volume. When the loss of secretions is more prolonged but less acute, the combination of a primary loss of extracellular fluid in the secretions, with a secondary compensatory transfer of intracellular fluid out of the cells, may result in marked distortion of electrolyte and fluid equilibrium.

Oesophageal obstruction

Whether this is due to benign or to malignant disease, there is usually progressive reduction in food intake, leading to under-nutrition with reduction in lean tissue mass and fat. If the findings of McCance (1951) can be applied to the under-nutrition caused by oesophageal obstruction, there will be an increase in extracellular fluid and a reduction in intracellular fluid which will be exaggerated by reduction in the serum-protein concentrations or by any large increase in sodium intake. The appearance and disappearance of visible oedema in under-nutrition are connected with posture and with the presence of a large volume of extracellular fluid which is free to move under the influence of gravity. These undernourished patients have a poor tolerance for intravenous infusions and for transfusions of blood or plasma, cardiac failure due to overloading being readily produced by small volumes of fluid. During recovery from under-nutrition there is an increase in intracellular water, protein and fat, and a decrease in extracellular fluid Because of their poor tolerance to intravenous infusions, the best way to improve the general state of patients with oesophageal obstruction before operative treatment of the obstruction is by feeding them through a jejunostomy (*see* page 134) supplemented by repeated slow small transfusions (500 millilitres) of fresh whole blood. Because the intestines are empty and contracted, only small frequent jejunostomy feeds, of 60 millilitres every hour, should be given for the first two or three days.

Loss of gastric and intestinal secretions

Rapid depletion of extracellular fluid volume may be caused by repeated vomiting due to pyloric stenosis or intestinal obstruction, by large fluid losses from duodenal, biliary or pancreatic fistulae, by diarrhoea from an ileostomy or colostomy, or because of irritation of the rectum by a pelvic abscess.

Loss of gastric secretion.—Vomiting in pyloric stenosis results in a large loss of chloride giving rise to compensatory alkalosis, but there is an accompanying loss also of sodium and potassium leading to a reduction in total base and therefore in body water (*see* Table III). The concentrations of these ions in gastric juice are such that one litre of gastric juice may contain as much potassium as 2–3 litres of plasma or [illegible]

but the chloride replacement will require 9 grammes (153 mEq.) of sodium chloride and the potassium 1 gramme (13 mEq.) of potassium chloride. The intravenous infusion of a litre of isotonic saline (0 9 per cent) thus provides a large excess of sodium but no potassium, and is clearly an inaccurate way of replacing lost gastric secretions. Because of the replacement of sodium and water, the infusion of isotonic saline may be followed by obvious clinical benefit, although this may be of only short duration. In uninjured patients, renal readjustment can do much to correct the inaccuracies of saline therapy However, renal compensation is limited and cannot function efficiently in the presence of severe uncorrected alkalosis and potassium deficiency, therefore, the longer vomiting continues without potassium replacement, the less effective are both saline replacement and renal compensation.

Whenever vomiting has continued for more than one week or ten days, potassium deficiency as well as alkalosis should be suspected. Some indication of potassium deficit may be obtained from change in the general state of the patient, especially

imposed by the operation and subsequent *complications. The* patient with impaire renal concentration requires each day more water than usual, but he is also less able t respond rapidly and completely by diuresis to sudden increments of water. To avoi water retention, the provision of this extra water during the immediate post-operati period must be carefully controlled. It is unwise to increase suddenly the water intak in elderly patients with impaired renal function, but to administer isotonic saline o *sodium sulphate* solution in an attempt to compel diuresis is dangerous.

The influence of liver disease

It has been known for many years that acute liver disease causes a disturbance o water balance. This may be shown by oliguria or even suppression of urine during th most acute stage of the disease and by a delay in diuresis *after the consumption of* a large volume of water; the onset of diuresis is well known to be a common first indication of improvement in liver disease of many kinds. Labby and Hoagland (1947) suggested that normally the antidiuretic factor of the pituitary may be inactivated by the liver; impairment of this process by severe upset of liver function might therefore lead to water retention. Their conclusions were based on investigations of *patients with acute infective hepatitis, and it* may not *be entirely valid to apply them* to the early stages of liver disturbance due to biliary obstruction. When obstruction has persisted long enough to cause secondary parenchymal liver damage there is less objection.

In acute hepatitis there is an increase in extracellular fluid volume affecting both plasma and interstitial fluid volumes; red cell and whole blood volumes also are increased. The reduction in urinary sodium and chloride excretion with diminished urinary volume might be expected because of the inflammatory reaction in infective liver disease or biliary obstruction with infection, it occurs also when the liver is damaged by prolonged obstruction without infection. The plasma-sodium and chloride concentrations fall in spite of renal retention of these ions, possibly because of the larger water retention, as indicated by a fall in the packed cell volume. There is also reduction in plasma-protein concentration which usually affects albumin more than globulin; the importance of this as a factor in the shifts of fluid in liver disease is not well understood.

Patients with acute liver damage secondary to biliary obstruction often look remarkably well until improvement begins, as indicated by the onset of diuresis, then *within a day or two their faces become wrinkled,* their eyes sink in the orbits and they look ill and much older, although in other respects their clinical state has undoubtedly improved. This striking change in appearance is due to rapid loss of an accumulation [illegible] following the [illegible]

carefully recorded, because they will provide the [illegible] liver function. Because of *the delay in excretion of water,* great care must be exercised in the administration of fluid by any route to patients with disturbance of liver function, especially just before operation.

Disturbances due to loss of intestinal secretions

The effects of loss of intestinal secretions depend primarily on the rate and total volume of fluid loss. These secretions are *derived in the first place* from plasma, and [illegible] through a fistula, [illegible] fluid. Loss of [illegible] of fluid from [illegible] ous and con[illegible] ert the onset tinuous, transference of cell fluid makes little [illegible] of oligaemic circulatory failure due to the *reduction in* extracellular fluid and plasma

volume. When the loss of secretions is more prolonged but less acute, the combination of a primary loss of extracellular fluid in the secretions, with a secondary compensatory transfer of intracellular fluid out of the cells, may result in marked distortion of electrolyte and fluid equilibrium.

Oesophageal obstruction

Whether this is due to benign or to malignant disease, there is usually progressive reduction in food intake, leading to under-nutrition with reduction in lean tissue mass and fat. If the findings of McCance (1951) can be applied to the under-nutrition caused by oesophageal obstruction, there will be an increase in extracellular fluid and a reduction in intracellular fluid which will be exaggerated by reduction in the serum-protein concentrations or by any large increase in sodium intake. The appearance and disappearance of visible oedema in under-nutrition are connected with posture and with the presence of a large volume of extracellular fluid which is free to move under the influence of gravity These undernourished patients have a poor tolerance for intravenous infusions and for transfusions of blood or plasma, cardiac failure due to overloading being readily produced by small volumes of fluid. During recovery from under-nutrition there is an increase in intracellular water, protein and fat, and a decrease in extracellular fluid. Because of their poor tolerance to intravenous infusions, the best way to improve the general state of patients with oesophageal obstruction before operative treatment of the obstruction is by feeding them through a jejunostomy (*see* page 134) supplemented by repeated slow small transfusions (500 millilitres) of fresh whole blood. Because the intestines are empty and contracted, only small frequent jejunostomy feeds, of 60 millilitres every hour, should be given for the first two or three days.

Loss of gastric and intestinal secretions

Rapid depletion of extracellular fluid volume may be caused by repeated vomiting due to pyloric stenosis or intestinal obstruction, by large fluid losses from duodenal, biliary or pancreatic fistulae, by diarrhoea from an ileostomy or colostomy, or because of irritation of the rectum by a pelvic abscess.

Loss of gastric secretion.—Vomiting in pyloric stenosis results in a large loss of chloride giving rise to compensatory alkalosis, but there is an accompanying loss also of sodium and potassium leading to a reduction in total base and therefore in body water (*see* Table III). The concentrations of these ions in gastric juice are such that one litre of gastric juice may contain as much potassium as 2–3 litres of plasma or extracellular fluid, as much chloride as 1·5 litres of plasma, but as much sodium as only 250 millilitres of plasma. After loss of one litre of such gastric juice, the replacement of the sodium can be achieved with 2 grammes (37 mEq.) of sodium chloride, but the chloride replacement will require 9 grammes (153 mEq.) of sodium chloride and the potassium 1 gramme (13 mEq.) of potassium chloride. The intravenous infusion of a litre of isotonic saline (0·9 per cent) thus provides a large excess of sodium but no potassium, and is clearly an inaccurate way of replacing lost gastric secretions. Because of the replacement of sodium and water, the infusion of isotonic saline may be followed by obvious clinical benefit, although this may be of only short duration. In uninjured patients, renal readjustment can do much to correct the inaccuracies of saline therapy. However, renal compensation is limited and cannot function efficiently in the presence of severe uncorrected alkalosis and potassium deficiency; therefore, the longer vomiting continues without potassium replacement, the less effective are both saline replacement and renal compensation.

Whenever vomiting has continued for more than one week or ten days, potassium deficiency as well as alkalosis should be suspected. Some indication of potassium deficit may be obtained from change in the general state of the patient, especially

recent loss of appetite and energy. The serum concentrations of sodium, potassium, chloride and bicarbonate should be measured and an electrocardiographic tracing made. The pre-operative treatment of such a patient is designed to replace the potassium deficit as well as that of chloride, and the smaller loss of sodium. The ideal method is by the oral consumption of as full a diet as can be eaten, combined with the emptying and washing out of the stomach at night; a supplement of up to 12 grammes of potassium chloride per day should be added to the diet. In spite of reducing the daily loss of gastric secretions and increasing the intake of food, fluid and potassium by these means, there may be a further reduction in the serum-potassium concentration which is difficult to explain. It is reasonable to continue with this method of replacement if the general condition of the patient improves and the volume of gastric residue diminishes; if not, other methods of replacement must be employed. The institution of a jejunostomy allows of the provision of a full daily intake of calories and protein, together with ample potassium and chloride. Alternatively, and in any case if there is coma, extreme drowsiness or persistent vomiting in spite of gastric lavage, the lost water and electrolyte should be replaced by intravenous infusions. The replacement of potassium should precede that of sodium in order to correct the disturbances of cellular function due to the intracellular transfer of sodium. Before a solution containing a potassium salt is injected, a urine output at the rate of at least 500 millilitres per day or 20 millilitres per hour should be ensured, if necessary by the infusion of a 5 per cent glucose solution. Up to 2 grammes of potassium chloride in a 5 per cent glucose solution may be administered over a period of 4 or 5 hours, and up to 12 grammes may be given during the first 24 hours. Because of the dangers of intravenous administration of potassium, it is wise to change to the oral route as soon as possible.

Occasionally, after partial gastrectomy or gastrojejunostomy, the return of gastro-intestinal motility is delayed for more than 48 hours. Accumulation of fluid in the stomach and upper jejunum then requires aspiration and the restriction of oral fluid intake. Usually this state lasts for at most a few days, but rarely it may persist for one week or more and then becomes a very serious complication. The cause of this impaired motility is uncertain; depression of the serum-calcium concentration, low plasma-protein concentration, administration of excessive quantities of saline and potassium depletion have all been suggested as causal factors. When, because of fear of an organic obstruction, the abdomen is reopened, the stomach and jejunum are usually seen to be immobile and stiff with oedema fluid, the stoma is widely open and across it fluid contents swill to and fro with each respiratory excursion. Restriction of the oral fluid intake is not always followed by reduction in the volume of the gastric aspirations. The stomach tube should always be withdrawn as soon as the fluid smells clean and is not thickly turbid. Intravenous saline administration should be strictly limited to a daily quantity sufficient to replace the sodium lost in the aspirated fluid, and the effect of an infusion of potassium chloride should be tried. It is doubtful whether any additional anastomosis should be carried out in the absence of organic obstruction; indeed, reopening of the abdomen and the inspection of the stomach and jejunum alone are often followed by early resumption of normal peristalsis.

A [illegible] lation of secre- [illegible] for a week or more, it may be due, at least in part, to depressed intestinal motility secondary to potassium deficiency. Webster, Henrickson and Currie (1950) produced potassium deficiency in rats by feeding them, for periods of at least a month, on a diet deficient in potassium; the rats showed gross disturbances of intestinal motility and distension of the intestines with gas and fluid, which responded to potassium therapy.

In such long-term cases the intravenous administration of potassium salts should be tried, success being usually indicated by an early increase in bowel sounds and by the passage of flatus.

The ileus which is associated with peritonitis may be of a different nature; the affected intestines are oedematous and stiff as they lie involved in the inflammatory mass, and peristalsis is sluggish. This local oedema of the bowel wall may be increased and its resolution and the return of normal peristalsis may be delayed, by the excessive administration of saline.

Loss of intestinal secretion.—When secretions from the small intestine are lost, there is a relatively larger depletion of sodium than of chloride and a loss of potassium, the total effect being a larger loss of base than of acid. The composition of vomitus or gastric aspirations in patients with *intestinal obstruction* or *ileus* varies with the proportions of gastric and intestinal juices, bile and pancreatic secretions which make up the fluid mixture which is removed; but, in general, the lower the site of the obstruction the greater is the tendency to acidosis. The fluid which is lost from a *duodenal fistula* is alkaline and contains little chloride; large quantities of base, chiefly sodium, are lost from such a fistula and lead to acidosis and reduction in extracellular fluid volume. A complete *biliary fistula* also produces severe fluid disturbances since, apart from the bile pigment, the composition of hepatic bile is almost the same as that of isotonic saline to which about 5 mEq. of potassium per litre have been added. *Pancreatic juice* alone may be lost from a fistula of an accessory duct or very rarely of the main duct. This juice is alkaline, but contains sodium and potassium in about the same concentrations as those in plasma.

In each of these types of loss of secretions the intravenous infusion of isotonic saline produces immediate improvement, because it replaces sodium and water. The excess of chloride administered in the saline may be excreted in the urine even when, because of a remaining sodium deficit, the plasma-chloride concentration is below the normal limit. The chloride administered in the saline increases the existing acidosis and the sodium increases the urinary loss of potassium.

Gastric, duodenal, biliary or pancreatic fistulae are rare but highly dangerous complications of partial gastrectomy for duodenal ulceration. Their recognition is usually made easier by drainage of the original operation wound which also reduces the extent of the intraperitoneal reaction when the leakage begins. The daily volume of fluid lost from these fistulae is proportional to the extracellular fluid volume, and is thus directly affected by the degree to which intravenous replacement succeeds in correcting previous losses of fluid. Although some of these fistulae dry up and close after periods of only 10–14 days without particular difficulty being encountered in their management, most persist for much longer periods and cause great anxiety and difficulty in their treatment, much of which can be avoided by the prompt institution of a jejunostomy within the first week after onset of the fistula. Such an early decision is essential if secondary disturbances due to intravenous replacement of electrolyte and fluid losses, and impaired healing of the jejunostomy wound, are to be avoided. The greatest advantage of the jejunostomy is that by enabling the direct replacement into the intestine of all the discharges collected from the fistula, complicated intravenous replacement is avoided, at the same time, because the full calorie and water requirements can be readily supplied, oral intake can be stopped entirely and the fistulous discharge correspondingly reduced. A jejunostomy is of no value when there is an intestinal fistula lower in the small intestine, or in the presence of a colostomy.

In *ulcerative colitis* there is a loss of mucus, purulent discharge and blood. The treatment of repeated losses of this nature requires transfusion of fresh whole blood as well as the administration of potassium citrate and sodium bicarbonate supplementary to the sodium and potassium salts consumed in the food. Replenishment of extracellular fluid by intravenous infusion also is required after large losses of fluid. After

the establishment of an ileostomy, bursts of diarrhoea are common and rapidly deple the already low extracellular fluid volume of these thin and ill-nourished patien Diarrhoea may rarely endanger life soon after the opening of a colostomy. In ea type of case, acidosis with severe depletion of sodium results and there may marked reduction in plasma volume; unless it is replaced, potassium depletion i creases with each successive attack.

Following *bilateral transplantation of the ureters* to the colon, all the urine is di charged into the bowel, and it has been known for many years that acidosis mig result from this deviation of the urinary stream, and that later dilatation of the urete was commonly followed by impairment of renal function. More recently it has becom evident that in a proportion of patients acidosis may be accompanied by other feature and further investigation has shown that there is wide variation in the clinical pictu and in the associated biochemical changes in these patients. At any time after operatio there may be a clinical disturbance varying in severity from slight thirst and tiredne through increasing degrees of muscular weakness, loss of weight and thirst to polyuri and diarrhoea, nausea, vomiting, prostration and coma. In about 80 per cent of case (Ferris and Odel, 1950; Jacobs and Stirling, 1952) the serum-chloride concentration raised and the alkali reserve is lowered; in some cases there is also an increased serum sodium concentration, and in a few serum-potassium concentration is lowered. Thi disturbance is exhibited only by continent patients after complete diversion of th urine to the large bowel.

There is much difference of opinion as to the primary cause of these disturbances The most widely accepted explanation is that the acidosis is due to the selective reabsorp tion of chloride from the urine in the colon; it has also been suggested that the caus is impairment of distal tubular function resulting from back pressure and *hydro* nephrosis, or from pyelonephritis due to ascending infection. The accumulation of urin for four or five hours or more in the colon above a continent anal sphincter seems to b an important factor whatever the remainder of the mechanism may be, and th continuous drainage of the colon through a rectal tube is one of the first steps to b taken in the treatment of severe acidosis which is completed by the *administration of* mixture of 30 grains of potassium citrate and of sodium bicarbonate every four to si hours and, if necessary, the restriction of the consumption of table salt. Occasionally patients are admitted in coma with which is associated an *intense chloride acidosis* and lowered serum-potassium concentration. This requires urgent treatment by the *intravenous administration of potassium and lactate as Darrow's solution*, even in the absence of an apparently adequate urinary output; as soon as possible potassium citrate should be administered by mouth in large doses (*60 grains every 4 hours*).

Shock

[illegible] closely follow injury; [illegible] ninant mechan- ism concerned in its production in any particular case, [illegible] "shock due to blood loss".

Classification

Shock was formerly classified according to the *time of occurrence* into primary shock, appearing within two hours of injury; and secondary shock, coming on more [illegible] took no account of the mechanisms [illegible] regardless of the [illegible] lished. Two main types may be recognized: (*1*) [illegible] e"; and (2) shock due to fluid loss, either (*a*) blood, or (*b*) plasma.

Neurogenic shock.—This may follow accidental bleeding or the bleeding of transfusion donors; it may be associated with emotion, manipulation of injuries such as fractures, or with change in posture. There is a fall of systolic blood pressure to about 60 millimetres of mercury and the diastolic pressure may be too low to be recorded; at the same time the pulse rate falls to 40 or 50 per minute. This reaction is due to vasodilatation of the arterioles of the skeletal muscles by nervous impulses mediated through autonomic fibres in the mixed peripheral nerves (Barcroft and his colleagues, 1944) Amongst blood donors the incidence and severity of the reaction are related to the quantity of blood which is removed. Recognition of this disturbance depends on observation of the very slow pulse rate combined with the low systolic pressure. The skin is usually pale and may be warm. Recovery may follow lowering the head, but this may make little difference The administration of a vasoconstrictor drug such as Methedrine (N-methyl emphetamine) usually constricts the dilated vessels in the skeletal muscles and returns the idling blood to active circulation.

Shock due to fluid loss.—Because there is loss of blood or plasma or both, out of the vascular system into the wound or damaged tissue, there is reduction in the volume of blood in active circulation within the vessels. It is now generally agreed that this extravascular loss of blood or plasma is the most important single factor in causing the syndrome of shock, and it follows that rapid and complete replacement of this loss is the chief factor in the successful treatment of shock due to blood or plasma loss.

In *shock due to blood loss*, the rate of loss is usually the overriding consideration, for whereas more than a gallon (4·5 litres) of blood in all may be lost over a period of several months from bleeding haemorrhoids or a carcinoma of the caecum—the daily loss being not more than an ounce or two—the rapid loss in a few minutes of only 2 pints (about 1 litre) may cause severe circulatory disturbance. Compensation for acute blood loss by the formation of red cells is slow, and restoration of volume by transfer of interstitial fluid into the vessels is partial and takes 24 hours or more to be effective. Reflex vasoconstriction reduces the capacity of the vessels and redistributes the remaining available blood to maintain an adequate blood supply to those organs and tissues on which survival of the organism primarily depends. This implies intense vasoconstriction in the less essential organs or those which, because of less highly specialized function, can continue to exist at a lower rate of oxygen turnover. The general vasoconstrictor effect of blood loss may be overcome locally by a strong stimulus like heat, as in the improvement in the rate of venous flow brought about by warming the limb before transfusion or by warming the fluid to be injected

In assessing the condition of a shocked patient and the rate and direction of change in his condition, some direct index of the circulatory state is needed. The best would obviously be a technically easy means of rapid and accurate measurement of total blood volume; at the present time no method exists which is suitable for general ward use by persons who have not learned the required special techniques. It is still necessary to make a clinical judgment based largely on past experience. The clinical data required are a history of the accident, the amount of blood lost, the nature and extent of the injuries, the systolic and diastolic blood pressure, the pulse rate and the colour and temperature of the skin in various sites, and the rate of return of skin colour after digital compression. By repeated observation of these clinical features at intervals of half an hour, or less during critical periods of rapid change, it is possible to build up a picture of the disturbance in a particular patient. Since no two shocked patients are ever wholly alike, this direct observation provides a more individual approach than any system based on a full description of many types of reaction.

The effects of an acute loss of blood vary greatly. In a fit young man with an initial blood volume of about 5 litres (8 pints):

(1) Up to a pint of blood may be lost without much change in the colour or temperature of the skin, pulse rate or blood pressure.

(2) After 2 pints of blood have been lost, the skin usually becomes pal cold because of cutaneous vasoconstriction, the pulse rate rises to abo per minute and the systolic blood pressure falls to about 100 millimet mercury.

(3) When the blood loss exceeds 3 pints, the increasing vasoconstriction pallor with cyanosis which affects even the lips, the pulse rate usually rises r and the systolic blood pressure falls below 80 millimetres of mercury, the di pressure may be too low to be recorded, and later the pulses may become in able. The patient is often mentally alert or euphoric, talkative and exubera perhaps excessively apprehensive. As his general condition deteriorates he become restless, exhibit air hunger and even maniacal excitement. In the ter stages, after rapid loss of very large quantities of blood, respiration becomes ga and spasmodic, consciousness may be lost and death may seem to be immi Provided that this state is of only short duration, complete recovery may f rapid replacement of the lost blood by transfusion.

The vasoconstrictor reaction may at times exceed the exact degree of inte necessary to compensate for the particular fluid loss which has occurred; this c what is known as the hypertensive response or reaction. This is more comm young subjects, especially children; pallor is usually marked, the extremities are and the pulse rate is increased. The hypertension may be suddenly succeeded profound fall in blood pressure, especially if the patient is warmed. A hyperte reaction should, therefore, always be an indication for caution and careful observa Patients who have been excessively chilled are, in general, more difficult to resusci it is often hard to predict how they will respond.

The commonest type of accidental injury giving rise to shock is a *wound of the l* especially in association with a compound fracture. The severity of the shock is re directly to the volume of blood which is lost from the circulation, which in tu usually related to the mass of muscle involved. Shock is therefore most seve association with lacerated wounds of the upper thigh and buttocks, and in comp fractures of the shaft of the femur. Grant and Reeve (1941) suggested that a quan tive estimate of the tissue damage, and so, indirectly of the blood loss, might be obta by estimating wound size in units of the size of the open hand or closed fist, whi about equal to 500 millilitres. In closed fractures, blood loss may also be calcul from measurements of change in the length and girth of the limb compared with t of the uninjured side. Bleeding is due chiefly to laceration of the surrounding mu bellies by the sharp and jagged ends of the broken bone. Fractures of the fem shaft associated with severe violence may be followed by the loss of up to 5 pint blood; bleeding is increased by movement of the fractured bone or the affected l and is minimized by early immobilization with some traction in a suitable sp Division of main vessels in limb wounds is comparatively uncommon in peaceti but extensive venous bleeding may follow injuries of the arms brought about glass.

Abdominal wounds are a common cause of severe blood loss during warfare; t have a variable incidence amongst civilians related to the freedom with which pis and knives are used. Bullets and other missiles with a high initial velocity may inj any abdominal organ and often pursue unexpected courses after penetrating abdominal wall. Because of the frequency with which mesenteric vessels are divid severe blood loss is common, but injuries of the great vessels within the abdomen comparatively rare. Before laparotomy, therefore, a hopeful attitude should maintained towards all cases of intra-abdominal bleeding. Direct blunt injury to abdominal wall and lower chest wall may cause severe laceration or rupture of liver, kidney or spleen with subsequent immediate, rapid and extensive bleeding. concealed or delayed bleeding. In all these injuries the cause of shock is predominan

loss of blood, and recovery should follow timely arrest of the haemorrhage, combined with adequate replacement of the lost blood.

The most important factor in the *shock due to plasma loss* following thermal injury is the loss of plasma from the heat-damaged capillaries in the injured area. This plasma loss occurs at the raw surface into the superficial blisters and into the underlying tissues It is most severe in superficial injuries in which the abundant skin capillaries are damaged but not destroyed by coagulation. The more extensive the superficial injury the greater will be the plasma loss and the more profound will be the shock. In deep injuries, in which the whole thickness of the skin is coagulated by the intensity or duration of the heat, the skin capillaries and their contained blood also are coagulated and plasma loss is confined to the marginal areas of superficial injury.

Because the loss of plasma leads to increasing haemoconcentration, it is generally believed that serial haemoglobin estimations will give a reliable indication of the severity of the plasma loss, and of the rate and direction of change in the condition of the shocked patient. It seems unwise to rely solely on one index when other simple bedside observations will provide additional valuable evidence. As in shock due to loss of whole blood, the state of the peripheral circulation in the ear lobes or in the nail beds of the fingers and toes, the rate of return of colour after digital compression, systolic and diastolic blood pressure and pulse rate should all be recorded and considered when the progress of burned patients is being judged.

Plasma loss begins soon after injury and may continue for up to 40 hours, but the chief loss occurs during the first 12 hours and this is also the time when shock is more severe and dangerous. At first blood pressure is usually maintained by vasoconstriction, and in children this may sometimes be excessive and lead to hypertension. As the plasma loss increases, compensation becomes less effective, the pulse rate tends to increase, and then, following a rise in diastolic pressure, there is a sharp fall in both systolic and diastolic pressures. Unless the lost plasma is rapidly and completely replaced, there is progressive deterioration as plasma loss continues, and in extensive superficial injuries death may occur at any time after 12 hours.

In those patients who survive, fluid loss into the injured tissues continues at a diminishing rate for up to 40 hours. The exudate begins to resolve after about 48 hours and from this time there is obvious reduction in the size of the local swelling with wrinkling of the overlying skin, crust or eschar. The fluid is absorbed into the capillaries or lymphatic vessels, and there is consequently an increase in blood volume followed by a diuresis from about 60 hours after injury onwards It is at this stage that the adverse effects of previous excessive infusions of fluid become most serious, the greater size of the burn exudate, due to the injection of large volumes of isotonic saline during the first 48 hours, results in circulatory overloading and oedema. If large volumes of glucose solution have been employed in vain attempts to induce diuresis, there may be marked dilution of the extracellular fluid. The systemic disturbances which may arise between 40 and 120 hours after burning have still not been satisfactorily analysed. The "acute toxaemia" which Wilson, MacGregor and Stewart (1938) described, and which has been attributed to the effect of absorption of toxic derivatives of tannic acid, has not been observed with other coagulants such as silver nitrate, but disturbances associated with other methods of local treatment, which somewhat resemble "acute toxaemia", have been reported.

The stupor, drowsiness and other mental disturbances, vomiting, reduced urinary output, rising body temperature, pulse and respiration rates suggest some disturbance of body-fluid equilibrium. This may be either water retention with sodium dilution or an excess retention of both sodium and water.

The object of treatment is to maintain oxygen carriage, if possible by preventing reduction of blood volume or by restoring blood volume when this is reduced. Formerly, the local application of tannic acid or silver nitrate solutions to the burned surface

was believed to be an essential part of treatment in that the surface loss of plasma was reduced. Such local applications do not affect the much larger loss of plasma into the burned tissues which is the cause of the swelling of the injured areas. Now that local coagulant therapy has been abandoned in favour of exposure of the raw surface or the application of ointment or pressure dressings, it is perhaps more than ever essential that circulating blood volume should be maintained by restoration of plasma volume by the early and rapid infusion of adequate volumes of plasma, or a plasma substitute such as gum acacia or dextran. There seems to be no justification for administering saline, because it will be so rapidly lost from the circulation, especially in the burned area, that it can increase the plasma volume for only a very short time; moreover there will be a large increase in the size of the burn exudate. In extensive deep burns there may be sufficient loss of red cells by coagulation in the burned area to require the transfusion of whole blood in addition to plasma or a plasma substitute.

Factors predisposing to shock

Any factor which minimizes or interferes with the immediate normal reaction to injury with blood or plasma loss may increase the severity of the shock. Neurogenic shock may be induced or aggravated by fear or pain. Pre-existing reduction in body water and especially of extracellular fluid reduces the fluid available for compensatory transfer after bleeding or plasma loss. Exposure to cold may increase the intensity of vasoconstriction and usually makes later resuscitation more difficult. A hot environment may impair the general vasoconstrictive response to injury and survival may be shorter; excessive heating of the shocked patient under "shock cages" or "cradles" by abolishing cutaneous vasoconstriction may cause a fall in blood pressure and may increase bleeding or plasma loss. Other injuries such as those of the chest wall or lung, brain or spinal cord may hinder the treatment which might otherwise be employed for shock or may complicate operative measures or anaesthesia.

Any rough handling of injured limbs or compound fractures tends to increase bleeding and tissue damage, and to cause further nervous stimulation. The shocked patient is peculiarly sensitive to changes in posture and position and tolerates badly sudden shifts or rolling; rapid levelling of the table at the end of even a short operation may cause marked deterioration in the condition of a shocked person. Gentleness and the elimination of unnecessary manoeuvres are essential during operation on severely injured patients. The shorter the duration of the operation consistent with thoroughness and gentleness the better, but speed alone is not enough; traction on mesenteries and interference with the upper abdominal organs cause depression of blood pressure, presumably by autonomic reflexes.

Diagnosis

In accidental injuries it is important to make a complete examination of the whole body as soon as possible. Clothing should be cut off, note being made of the quantity of blood on the garments, dressings and stretcher. If not already done, fractures should be splinted and bleeding controlled by pressure with pads. The most important evidence is the size of the wound, for it is seldom that blood soaking of clothes or dressings indicates accurately the whole volume which has been lost. A large wound is usually a good indication for starting a transfusion as a precaution. Apart from this, a systolic blood pressure level of 100 millimetres of mercury is an indication of moderate shock; of 80 millimetres of mercury, of severe shock; and below 80 millimetres of mercury, of very severe shock. In general, it is wise to transfuse all patients whose systolic pressure falls below 80 millimetres of mercury because of blood or plasma loss.

[illegible] recommendations is in the case of vasovagal or neuro-
[illegible] nd that due to blood or plasma
[illegible] pulse rate and the state of the

skin. In vasovagal shock the systolic blood pressure may be 60 millimetres of mercury and is associated with a slow pulse rate in the region of 40 or 50 beats per minute, the skin is pale but warm. In shock due to loss of blood or plasma the systolic blood pressure is not often as low as 60 millimetres of mercury, the pulse rate is fast, 100–120, and rarely even 140 beats per minute, the skin is pale and cool or cold. A vasovagal reaction may develop during or soon after surgical operations and general anaesthesia; because of blood loss a mixed picture is produced, the blood pressure being unexpectedly low for the observed blood loss and the pulse rate faster than would be expected for a pure vasovagal reaction.

The unusual combination of a normal blood pressure with severe injuries is usually an indication of a hypertensive response and special caution is required; the pulse rate is usually raised and the skin is pale and cold. When a small wound is associated with an unexpectedly low blood pressure, the pulse rate often provides the clue to a correct diagnosis. If the pulse is very slow, a vasovagal reaction is indicated and external blood loss has probably been very small If the pulse rate is fast, it suggests either a poor vasoconstrictive response or the impairment of this by heating. Another possibility is that severe blood loss has occurred, and may have been due to injury to a large artery or vein.

Prognosis

Age.—Because of the higher surface-area-weight ratio, the cutaneous circulation is more important in children than in adults, in whom burns are proportionately more serious than in adults, and interference with vasoconstriction by excessive warming is more harmful. It is also true that children and young adults respond more readily and completely to thorough treatment of severe shock and extensive injuries than do older subjects.

Time.—The sooner the injuries are treated and the fluid loss is replaced the better the prognosis. Delay is of no value in the treatment of shock, although it may occasionally [illegible] Low bloc [illegible]

S[illegible] ith a bad prognosis because of the associated large blood loss and the difficulty involved in adequate haemostasis and treatment of the wounds. Such wounds are those of the buttock and upper thigh and the internal lacerations associated with severe and bilateral fractures of the pelvis. Injuries resulting in the pulping of large masses of muscle lower in the thigh or in the calf are associated with severe shock, which is often resistant to transfusion until the pulped muscle has been excised. The shock associated with extensive lacerations and the raising of large flaps of skin by oblique crush injuries in "run-over" accidents also may be resistant to transfusion before operative treatment of the injuries has been carried out. Multiple limb injuries, such as compound fractures, are sometimes best treated in stages, for the additional blood loss associated with excision and suture of the wounds may render immediate manipulative reduction of the fractures unduly dangerous; it may sometimes be wiser [illegible]

Chest injuries alone usually do well and shock is not severe, but when combined with abdominal or limb injuries they impose some limitation on the freedom with which blood and other fluids may be transfused.

Treatment

General principles.—It seems hardly necessary to emphasize that the treatment of patients shocked by blood loss from severe or extensive injuries comprises more than

just the replacement of the lost blood. It is essential to visualize at the outset the whole process which may be involved in the treatment of a particular patient. Only in this way can decisions be made as to how much blood will probably be necessary, how long resuscitation may take, at what point immediate operation becomes more important to survival than continued transfusion alone, and the amount of further bleeding and injury which may be inflicted by operation. Once having made such an assessment, the surgeon must be prepared to modify the original estimates and decisions as treatment progresses according to the response of the patient, for the shocked patient is liable to rapid deterioration and improvement. The management of the severely wounded patient demands continuous close attention, repeated measurement of pulse rate and blood pressure, and observations of the cutaneous circulation and general state. The sooner operative treatment can be carried out the better, and damaged tissue should be removed as soon as possible. When a number of shocked patients are admitted at the same time, decision as to priority depends to some extent on the nature of their injuries, but the rate at which they can be resuscitated may vary and may prove the more important factor.

In ideal circumstances the surgeon should conduct the resuscitation of the patient as well as the operative and post-operative treatment. Close co-operation between surgeon and anaesthetist is essential, and if the surgeon is unable personally to supervise resuscitation, the anaesthetist is the best alternative person to do so. It is usually easy to recognize when the condition of a patient has been restored to normal by measuring pulse rate and blood pressure and by observing the other signs of circulatory improvement, and with reasonable precautions the subsequent management of such patients does not give rise to difficulty Unfortunately, many patients with severe injuries do not respond so completely or in a consistent fashion to transfusion and in these circumstances difficult decisions must be made. For example, a patient with a gunshot wound of the abdomen may respond well to the rapid transfusion of three pints of blood during a period of 45 minutes, then blood begins to flow from the small wound of entry and blood pressure which had risen from an unrecordable level to 100/50 millimetres of mercury once more falls. This deterioration continues in spite of an increase in the rate of transfusion It is obvious that intra-abdominal bleeding has restarted or has increased in rate, and equals or exceeds the rate of replacement by transfusion. The only worthwhile course is to proceed at once with laparotomy in the hope of being able to control the bleeding vessels, and then by rapid replacement of the lost blood by transfusion to make the remainder of the operation feasible and safe. An equally urgent decision may be required in the case of limb injuries where there is a large quantity of mangled muscle. In the course of resuscitation of such patients a peak of condition is reached which is soon followed by deterioration; although later, a further period of improvement may be achieved, the first peak of improvement is invariably the highest. The optimum time for operation is just before this peak is reached, its recognition demands calm assessment, rapid unfaltering decision and a willingness on the part of both surgeon and anaesthetist to accept the unusual risk.

General measures.—After arrival at hospital, a short period of rest for the patient is often followed by a marked improvement in general condition. It is important that he should be made as comfortable as possible Splints and dressings may require adjustment and the foot of the bed should be raised on 10-inch blocks. Reassurance of the patient is of the greatest importance, and he should be told something of the nature of his injuries. Morphine should not be administered except for the relief of pain, and should always be given in moderate doses (not more than ¼ grain) by deep intramuscular injection. Absorption from the subcutaneous tissues is delayed in severe shock and repeated doses may be absorbed simultaneously when blood flow improves after transfusion, leading to morphine poisoning. The slow intravenous

njection of morphine is permissible, but is dangerous in severely shocked patients because, on account of redistribution of the circulating blood by vasoconstriction, an ... may reach the central nervous system.

... possible and the patient should be placed in a ... t way to restore the peripheral circulation in a shocked patient and to make the skin warm and red is to replace the lost blood or plasma by transfusion. To heat such a patient with hot water bottles, electric blankets or "shock cradles" causes vasodilatation and is harmful, since it impairs the vasoconstrictive redistribution of the diminished blood volume on which survival may depend. Provided the patient is covered with enough blankets to retain body heat, he will ...

... with cold water. Large ... ely shocked patient, but ... l dangerous during the induction of anaesthesia. To avoid this danger, patients who have been allowed to drink should have their stomachs aspirated before anaesthesia is induced. Unless there has been a long delay between injury and arrival at hospital, few civilian patients in temperate climates suffer from such severe deficiency of body water, apart from that due to bleeding or plasma loss, as to require intravenous infusion of glucose solution or saline before operation. When there has been delay, the best pre-operative treatment is still probably adequate blood transfusion.

In hot climates and especially in the tropics, increased water loss by sweating may rapidly cause depletion and require replacement even before operation. The most important measures are those designed to prevent undue heating of the patient and excessive loss of water. The patient should be shaded from the sun and cooled by fans Intravenous infusions of glucose may be necessary if there is vomiting or if an adequate water intake is impossible because of the nature of the wounds. Saline should be used with caution, because of the retention of sodium and associated water by the injured subject Atropine should not be used in premedication Sweating during operation should be minimized by cooling the theatre and by dispensing with rubber ...

... deter- ... . Some improvement usually, and complete recovery occasionally, follows elevation of the foot of the bed. It is doubtful whether vasoconstrictor drugs such as Methedrine should be used in severely shocked patients Close observation combined with adequate replacement of any accompanying blood or plasma loss is probably the wisest course to adopt.

Restoration of blood volume.—Transfusion is indicated (1) in all patients with a pulse rate above 100 per minute and a systolic blood pressure below 80 millimetres of mercury, and in other patients when there is any doubt or if spontaneous improvement does not result from simple general measures; and (2) in the presence of severe injuries with tissue damage exceeding the size of two fists in volume, even when blood pressure is within normal limits and the pulse rate is not raised.

The lost fluid should be exactly replaced, blood for blood and plasma for plasma. Delay can be avoided by starting a transfusion with plasma or plasma substitute such as dextran or gum saline; these fluids may also be used instead of blood when only limited quantities of blood are available, or when only small volumes of replacement fluid are required (up to 1 litre, or 1¾ pints).

In deep burns there may be sufficient destruction of red blood corpuscles by coagulation in the burned tissues to warrant replacement by whole-blood transfusion. The former reluctance to use whole blood under any circumstances in the treatment of shock due to superficial burns has been shown to be unfounded. For the oligaemia

associated with peritonitis, ileus and strangulation of intestine, blood should be used.

The two factors, rate and volume, are to some extent interdependent. The slow transfusion of a very large volume of blood may be ineffective when the rapid injection of a small volume would have produced a marked improvement. The sooner transfusion is begun the more likely is the rapid administration of a small volume to be effective.

In severe shock the fluid should be injected as fast as it can be made to run through the size of needle employed. Pressure may be applied to the air inlet of the transfusion bottle. Venous spasm can be reduced by warming the limb and the blood or other fluid before administration. The arm veins should be used in preference to those in the legs, especially in abdominal injuries. By these means a pint of blood may be injected in five minutes, but such rapid replacement should not be continued after the systolic blood pressure has been raised to 100 millimetres of mercury. The total volume to be given to a particular patient depends on the quantity which has already been lost and on whether blood loss is continuing.

Until the original blood volume is restored, there does not seem to be much risk of overloading the circulation by fast or massive transfusions, for the normal cardiac functional reserve is able to deal with far larger temporary increases in output than are likely to result from transfusion to restore reduced blood volume. However, when blood volume is normal comparatively small increases in circulating volume may give rise to marked circulatory disturbance by overloading (Wilkinson, 1952).

Even when blood volume has been fully restored before the operation is begun, the intravenous infusion should be continued slowly during and for a time after operation, to enable the rapid replacement of any further blood loss to be made without delay. During the operation, the general progress of the patient is best judged by repeated measurement of blood pressure, pulse and respiration rates and observation of the state of the peripheral skin circulation. The colour of the blood and the rate of bleeding may provide some additional information. Most of this must necessarily be done by the anaesthetist who is also in the best position to assess the effects of the anaesthetic agents on the circulatory and general state of the patient. It may be necessary at times to stop manipulation in the upper abdomen or of a fractured limb because of the neurogenic hypotension which this may cause. Whatever may be their [illegible] ment of lost blood may have been inadequate and the residual vasoconstriction on which circulatory efficiency depends may be abolished by these hypotensive agents. This risk is not outweighed by the possible reduction of operation blood loss at a lower blood pressure.

After operation a slow intravenous infusion of glucose solution is usually continued for 12–24 hours so that any further blood loss may be replaced without delay. In chest injuries only the minimal quantity of blood should be employed and the infusion should be stopped as soon as blood loss has been replaced. In abdominal injuries involving the alimentary tract, the oral intake of fluid is usually restricted or stopped for 24 hours or more and gastric aspirations are instituted. Fluid intake is generally maintained by intravenous infusion until the oral intake of fluid can be resumed. In burns, the blood pressure should be restored by the rapid intravenous injection of dextran and then the vein kept open by a very slow infusion of glucose solution. Further dextran may then be administered immediately it is needed and the basal requirements of water can be satisfied by the glucose infusion.

During an operation such as that of synchronous combined abdominoperineal excision of the rectum it is sometimes found that severe blood loss causes hypotension which does not respond even to the transfusion of a greater volume of blood than has been lost. In such cases there is often a remarkable response to the rapid infusion of

dextran or gum saline (Wilkinson, 1951). The reason for this response is unknown; it begins after only a small volume of dextran or gum saline has been administered and seems to be related rather to some property of the agent than to the volume of fluid employed.

Prevention of shock in deliberate surgery

General measures.—The patient should be brought to operation in the best possible condition and all unusual and violent methods of preparation, such as repeated drastic purgation which might disturb his fluid equilibrium, should be avoided. Restriction of food and fluid intake should be reasonable and mobility maintained as long as possible. Blood volume should be restored and anaemia corrected by transfusion, and disturbances of water, sodium, potassium, chloride or bicarbonate equilibrium should have been corrected and an interval allowed for stabilization before the day of operation

Hypotensive procedures designed to limit blood loss have been used for many years, but some consideration of recent additions seems worthwhile. Spinal analgesia produces arterial hypotension by vasodilatation in the distribution of the spinal segments affected by the drug. The resulting diminution in bleeding in the operation wound has been of value in many operations and the recent extension of this method to very high (T2) spinal block has provided bloodless fields for such operations as splachnicectomy. A similar reduction in blood pressure may be achieved by the use of the methonium compounds in suitable dosage. The advantages of these methods are · first that blood loss being reduced, blood transfusion is less often necessary; and secondly, smaller doses of anaesthetic drugs are required to produce particular effects than in normotensive patients, and recovery from anaesthesia is usually more rapid. These methods are not without risk, and the chief disadvantages are the difficulty of precise control and judgment of the individual dose required, some patients badly tolerate hypotension of this type and there are occasional failures to recover to normal blood pressure levels after operation. Their use is contra-indicated in children, and in frail or cachectic patients in whom a diminished blood volume maintains circulatory efficiency only with the aid of vasoconstriction, and in shocked patients in whom there is compensatory vasoconstriction.

To reduce bleeding from certain cerebral tumours, blood may be withdrawn into a sterile container before the operation is started, and in addition the patient may be operated upon in the sitting position. At the end of operation the blood which was withdrawn is reinfused.

Crush syndrome (ischaemic muscle necrosis)

This syndrome consists of prolonged crushing injury of a limb with pressure necrosis of muscle followed by anuria and renal failure after release from compression. Originally described by Frankenthal (1916) this condition was encountered in between 1 and 5 per cent of British air raid casualties admitted to hospital (Bywaters, 1944). It is rare in peace-time, the commonest cause then probably being compression by roof falls in mining accidents The typical pathological features, ischaemic muscle necrosis and myohaemoglobinuria, have been found after other types of injury, such as lesions of main vessels or fractures, in which mismatched transfusion or sulphonamides could be excluded as important factors in the associated anuria.

Release from compression may take many hours. By the time the patient arrives in hospital there may be a zone of erythema at the margin of the compressed area, or this may appear only after warming or resuscitation. Blistering may later appear in the normal skin adjacent to the compressed area, which remains pale grey and opaque like a deep burn. Within an hour or two of release the general state deteriorates as the result of plasma loss into the damaged crushed tissue which swells. For a time,

as in burns, the blood pressure levels are maintained by vasoconstriction ...

... tense skin, the distal pulses may disappear. On incision of the swollen limb, serous fluid oozes from the oedematous subcutaneous tissues; when the muscle fascia is opened, friable, wet, greyish, swollen muscle bulges outwards. The urine first passed may be normal, having been secreted before injury, but thereafter it is highly acid (*p*H 5) and contains albumin and muscle pigment. As renal failure comes on, both the volume and specific gravity of the urine fall and acid haematin is found in the dark deposit. There is progressive nitrogen and potassium retention, and unless there is a large diuresis death will occur after about a week from excessively high extracellular potassium concentration. At autopsy, the cortex of the kidneys is ...

... urine without deposit but pink in colour due to dissolved oxymyohaemoglobin, and albumin is present.

This syndrome consists of two components: first, the loss of plasma into the crushed tissue after release of compression with the subsequent development of a form of shock due to plasma loss; and secondly, the excretion of oxymyohaemoglobin or metamyohaemoglobin in an acid urine. It appears that the combination of reduced renal blood flow, acidosis and pigment excretion is necessary for the production of the fully developed state.

Treatment is primarily the prompt replacement of plasma loss before there is depression of blood pressure, the early provision of adequate water for urine formation, and alkali as lactate or as bicarbonate to render alkaline any urine which is formed. The administration of water and alkali should be carefully controlled and restricted if a diuresis does not follow within an hour or two Otherwise, water retention may occur secondary to renal failure. Established renal failure should be treated as indicated in the section on anuria.

Anuria

Anuria due to acute renal failure may be encountered following a large variety of different primary conditions such as shock, surgical operations, mismatched transfusion, "crush syndrome", abortion, concealed accidental haemorrhage or prolonged renal ischaemia from any cause. Bull, Joekes and Lowe (1950) found a uniform pattern of disturbance of renal function in these conditions characterized by evidence of gross tubular dysfunction and extreme reduction in renal blood flow, and in the fatal cases by a typical pathological picture; they have applied the term "acute tubular necrosis" to the whole group instead of that of "lower nephron nephrosis" proposed by Lucké (1946).The anatomical lesion affecting all parts of the nephron is necrosis with subsequent regeneration of the tubular epithelium.

The clinical course can be divided into four stages (Bull, Joekes and Lowe, 1950):

(1) *Stage of onset.*—A period of severe and prolonged shock or diminution in blood flow, or a period during which a toxin such as mercury is acting.

(2) *Stage of anuria or oliguria.*—During this stage, lasting from 1 to 23 days, less than 300 millilitres of urine per day is secreted,

(3) *Early diuretic stage.*—This follows in patients who recover with a gradual or occasionally a sudden increase in daily urine output, the volume soon reaching a litre or more, but there is at first no evidence of tubular function.

(4) *The late diuretic stage.*—It is said that this stage is present when there is evidence of tubular function.

When renal blood flow is diminished in the stage of onset, it affects equally

glomerular as well as tubular function. When blood flow is restored, glomerular filtration is gradually resumed, but tubular function is more slowly regained. It is not known how long anoxia must last to produce tubular changes, but Darmady (1952) suggests on a basis of animal experiments that the critical time may be 6–8 hours. Undoubtedly, the prompt correction of hypotensive states will greatly reduce the incidence of renal disturbances and is the most important way of preventing tubular necrosis Tubular lesions have been described in association with severe alkalosis and potassium deficiency (Cooke and his colleagues, 1952), but are not identical with or so extensive as those in acute tubular necrosis. This distinction is important because recovery will follow replacement of potassium in the alkalotic disturbance. In the true acute tubular necrosis, potassium therapy is to be avoided because the retention of potassium during the oliguric or anuric stage itself constitutes a dangerous risk of potassium intoxication. Circulatory disturbances secondary to renal disease may result from excessive loss of sodium and water in the urine or by vomiting, and ultimately give rise to anuria. In all cases of anuria obstruction of the renal tract must be excluded or treated.

Impaired tubular function in the second and third stages is shown by inability of the kidneys to concentrate urea and creatinine, to conserve sodium and chloride, to extract para-amino-hippuric acid from the blood or to reabsorb glucose at a normal rate. There is a rapid initial loss of tubular function, but a very slow return beginning only after several days and becoming complete only after many weeks or months. During the anuric stage there is retention of potassium with the possibility of a toxic concentration being reached, and later, during the diuretic stage, a risk of a large and prolonged loss of sodium and chloride in addition to a continuing loss of potassium.

Treatment

The aim of treatment is to keep the patient alive until tubular epithelium regenerates. Any circulatory disturbance causing renal ischaemia must be corrected as rapidly as possible. Until glomerular filtration is re-established in the early diuretic stage, water, minerals and other substances cannot be excreted by the kidneys and, if administered in excess of the quantities lost by insensible loss and in the sweat, faeces or vomitus, will accumulate in the body. Diuretics which act by osmotic effect or on the tubules are useless and may be harmful in the anuric stage, which is also unaffected by spinal or splanchnic block or by decapsulation of the kidneys. During the early diuretic stage accurate measurement of the water and mineral loss is necessary if large deficits of sodium, potassium, chloride and water are to be avoided by suitable replacements or increased intake.

During the anuric stage water intake must be limited to 1,000 millilitres per day to supply sufficient water for extrarenal losses only. In this way water intoxication and extensive oedema can be avoided. Similarly, since apart from excretion in the urine the only ways in which sodium and potassium can be lost is by vomiting, in the faeces, or by sweating, there must be restriction of the intake of these elements until diuresis starts Acidosis and alkalosis cannot be corrected during the anuric stage and do not appear to influence greatly the prognosis at this time. Because of starvation there is catabolism of protein tissue with resulting accumulation of nitrogenous metabolites such as urea, and also of potassium. This protein breakdown can be minimized by the administration of a fat-glucose emulsion which provides a high caloric intake as well as the daily ration of water. Bull and his colleagues (1949) modified Borst's (1948) diet and recommended the administration of 400 grammes of glucose and 100 grammes of peanut oil, emulsified with acacia, in one litre of water. This mixture provides 2,300 calories per day free of protein and minerals and can be administered by a stomach tube for periods of up to three weeks. Vomitus must be collected, filtered and reinjected If vomiting is so persistent as to make intragastric

tube feeding impossible, a sufficient amount of a 50 per cent glucose solution should be administered through a polythene catheter passed until its tip lies in the superior vena cava (de Keyser and his colleagues, 1949); the immediate dilution of the glucose solution in a large stream of blood in this way avoids the thrombosis which renders more peripheral injection impossible. The use of more dilute glucose solutions would involve the injection of too large a volume of water. In spite of a high caloric intake, accumulation of potassium sometimes occurs, or this may result from the mistaken or ill-advised administration of potassium salts. An artificial kidney is seldom available and peritoneal dialysis is dangerous and not very effective. Some improvement may follow the administration of 50 units of insulin and 50 grammes of glucose (Bywaters and Joekes, 1948) which causes deposition of potassium in glycogen. Bull (1952) has recommended the use of an ion exchange resin, and states that with 200 grammes of Zeo-Karb 225 in the sodium cycle, 262 mEq. of potassium have been abstracted, whereas a 7-litre peritoneal dialysis removed only 17·4 mEq.

Most patients with anuria will be receiving injections of an antibiotic and may have been given a sulphonamide drug. Crystalline penicillin may safely be given in a daily dose of up to one mega unit. Streptomycin, chloramphenicol, aureomycin and terramycin, however, will soon cause toxic effects if their administration is continued, and a single dose will be sufficient to maintain an adequate concentration.

During the diuretic phase sufficient water to equal urinary volume is added to the basal 1,000 millilitres of water intake. Because of the rapid loss of potassium in the urine, potassium should be supplied in the form of fruit and fruit drinks, and if the serum concentration falls, as potassium chloride by mouth up to 6 grammes per day. The body content of sodium and chloride is similarly maintained by supplementary intake of sodium chloride as indicated by daily measurement of the serum-sodium and chloride concentration, and if possible by measurement of the urinary output.

TREATMENT OF FLUID AND ELECTROLYTE DISTURBANCES

Principles of replacement therapy

Fluid therapy should be designed to provide the normal daily requirements of water and electrolyte and to arrest, as far as possible, any deficits already taking place. It must be based on estimates of the rate of use of water and electrolyte and changes in body composition, evidence of fluid loss being obtained from the history of the illness and from clinical examination of the patient. Body-weight may give an indication of the total water state of the body, and the volume and composition of the urine may show how renal mechanisms have compensated for losses of body fluid. Changes in the serum concentration of sodium, potassium, chloride and bicarbonate will show what alterations have occurred in the composition of the extracellular fluid, and may give indirect evidence of changes in intracellular fluid. The response to treatment is judged also by the changes in the clinical state of the patient, by repeated estimations of serum-electrolyte concentrations, blood pressure, pulse rate and peripheral skin circulation, volume, specific gravity and composition of the urine, and if possible, by body-weight.

The cellular environment depends primarily on the maintenance of an adequate circulating blood volume. Transfusion of blood, plasma or a plasma substitute is therefore the first measure to be considered in all cases. Replacement of deficits of water and electrolyte is important, but in many surgical emergencies it is a secondary consideration provided blood volume is maintained. In diseases for which operative relief is less urgent, attention may be given to replacement of electrolyte deficiencies, but it should be recognized that time is required for the normal distribution of administered water and electrolyte in the body, and that whereas sodium deficiencies can be replaced in two or three days, at least a week or more may be necessary for the

slower process of potassium assimilation by the cells. In designing any required combination of fluids, care must be taken that provision is made for the secondary changes of acidosis or alkalosis, and that the replacement fluids do not themselves create further biochemical disturbances. In addition, water to cover the daily insensible loss and for urine formation, and 100 grammes of glucose daily to prevent ketosis and reduce tissue catabolism, must be provided. The complete and accurate intravenous replacement of lost body fluids is difficult and seldom possible for long periods; such losses should rather be limited by curtailing oral intake, and by other means.

Fluids injected into the blood stream are out of our control as soon as they leave the needle, and their fate and effects then depend on the conditions within the body. The only components of blood which will remain to any large extent within the vessels are the red blood corpuscles. Albumin is normally retained by the peripheral capillary walls, but passes freely through those of viscera such as the liver. After injury and during inflammation, in the affected areas even the peripheral capillaries are freely permeable to albumin and globulin. Crystalloid and glucose solutions rapidly leave normal capillaries until a new equilibrium is established in the extracellular fluid; in the absence of a diuresis this would imply the transfer of up to 75 per cent of such solutions to the interstitial fluid within about two hours of their infusion. In the normal uninjured adult, however, the rapid intravenous infusion of a 5 per cent solution of glucose is followed by a diuresis which soon equals the rate of infusion; isotonic saline produces a much less marked increase in urine volume. After severe injury the rate of excretion of glucose solution is slow, but infused saline is largely retained for several days.

The appropriate fluids will be discussed in four groups: (1) restoration and maintenance of blood volume; (2) provision of water; (3) replacement and maintenance of electrolytes, and (4) maintenance of nutrition.

Restoration and maintenance of blood volume

Acute reduction

Acute reduction of circulating blood volume follows severe bleeding due to accidental injury or surgical operation and is best corrected by the rapid transfusion of an equal volume of blood, plasma or a plasma substitute. Provided such replacement is early and adequate, it should not be necessary to transfuse additional blood unless bleeding recurs or is continuous. Plasma loss in burns should also be rapidly replaced by plasma or by a plasma substitute, but because of the continued loss of plasma for up to 40 hours after injury, further infusions may sometimes be required after extensive injuries. After loss of small volumes of blood of up to one litre, plasma or a substitute may be used instead of blood, but blood is often of value in extensive deep burns in which there has been destruction of whole blood.

Chronic reduction

Chronic reduction of circulating blood volume follows the repeated loss day after day for weeks or months of small quantities of blood from a gastric or caecal carcinoma

circumstances, increased cardiac output which depends on an elevation of right auricular and venous pressures, a type of compensatory "heart failure" which is liable to cause acute pulmonary oedema or auricular dilatation when the circulation is further overloaded by transfusion. This disaster can be avoided by the slow transfusion of a small volume of blood and by the close observation of the state of the neck veins of the patient.

It has been *frequently suggested that protein deficiency should be treated by the* intravenous administration of whole plasma or of concentrated plasma albumin. These proteins are only slowly metabolized in the body, but do not remain long in active circulation. Thus the initial increase in plasma-protein concentration which follows their administration is usually followed by a slow decline. A lasting increase in plasma-protein concentration cannot be expected from such treatment and will follow only a general improvement in the nutritional state of the body as a whole.

Because of the danger of inducing Rh-sensitivity in Rh-negative females before the menopause, particular care must be exercised in *the selection of blood for transfusion* into such subjects, and the transfusion should be begun with plasma or a plasma substitute while such blood is being tested. There is now sufficient evidence (*Brit. med J.*, 1952) *to require that such precautions be strictly* observed by everyone responsible for the administration of blood transfusions.

During the past five years the use of fresh or reconstituted plasma and serum has declined, probably largely because of the fear of reactions and of homologous serum jaundice and virus hepatitis. Over the same period some have turned again to gum acacia, but the introduction of dextran and polyvinylpyrrolidone has provided welcome alternatives to plasma.

Plasma substitutes

Plasma substitutes are fluids, such as gum acacia, dextran, gelatin or polyvinylpyrrolidone, designed to replace plasma or serum in the treatment of shock due to blood or plasma loss. They are necessary because supplies of both blood and plasma are insufficient to meet existing requirements and to provide a stored reserve supply for future emergencies To be effective, a plasma substitute must satisfy certain requirements. It must be non-toxic when injected in therapeutic quantities and it should

factory colloid osmotic pressure. While being retained in the blood stream long enough and at a sufficiently great concentration to cause a lasting increase in blood volume, the material should ultimately be completely excreted from or metabolized in the body.

Since the purpose of a plasma substitute is to increase the volume of circulating fluid, retention within the vessels of a high proportion of the administered dose is essential. This retention depends on the physical properties of the substance, the molecules of which must be of such a size and shape that they do not readily pass through the capillary wall. Size is on the whole the more important factor, but at certain critical points shape may determine whether the molecules of different substances of the same molecular weight pass through the capillary wall. All the plasma substances in use are colloids of large molecular size, and being prepared by chemical synthesis or degradation, they always contain a mixture of molecules of various sizes. The behaviour of a particular mixture depends on the relative numbers of molecules of various weights present in it. Immediately after injection, most of the injected material can be accounted for in the circulating blood. There is subsequently a loss of material from the blood, the rate and degree of which depend on the molecular composition of the injected material. Bayliss, Kerridge and Russell (1933) studied the excretion of protein in anaesthetized cats and rabbits and in the isolated perfused kidneys of dogs, and found that all the proteins excreted were of molecular weight less than 70,000, and all those retained had molecular weights exceeding 70,000. They further showed that it was the weight rather than the origin or nature of the molecule which was the critical factor in deciding whether the material crossed the glomerular membrane. Therefore it is not surprising to find that after infusion of a plasma substitute.

material of molecular weight less than 70,000 is rapidly excreted in the urine, and as excretion of these smaller particles becomes more complete, the rate of excretion [illegible] and the average size of the retained material increases

[illegible]

will gradually pass back into the plasma and be excreted in the urine.

The large urinary excretion of material of small molecular weight causes a diuresis and may lead to undesirable water and electrolyte loss. When there is a rapid loss of injected colloid in the urine, the increase in blood volume is of only short duration and repeated infusions may be necessary.

Material of molecular weight between 70,000 and 130,000 does not readily pass [illegible]

will remain in circulation until it is metabolized, excreted after partial breakdown, or deposited in the reticulo-endothelial cells of the liver, spleen and lymph glands. It is undesirable to inject material the molecular weight of which exceeds 250,000 because of the adverse effects caused, particularly marked aggregation of the red cells and undesirably great increases in erythrocyte sedimentation rate and viscosity.

The crude preparations of the materials commonly employed contain molecules of weights ranging from a few thousand to several millions. To obtain a preparation suitable for intravenous injection, the crude preparation must be hydrolysed to reduce the molecular weight. This results in a mixture of particles of smaller but of various molecular weights, which is then fractionated in various ways to produce a final product of the desired limited molecular weight range and composition.

The ideal preparation for producing a lasting increase in circulating volume should therefore contain minimal quantities of material with molecular weight below 70,000 which will be rapidly lost in the urine, and above 250,000 which will increase viscosity, aggregation and sedimentation of red corpuscles The bulk of the material should be in the range of 130,000–200,000; a proportion between 70,000 and 130,000 is permissible but should be as small as possible. The manufacture of such closely fractionated preparations is not easily practicable for some materials, and is always relatively costly in material and apparatus. The nearer the ideal is approached, however, the smaller are the losses into the urine and interstitial fluid and the less is the quantity which has to be injected to produce a satisfactory response.

Difficulties are encountered in the comparison of different preparations and of different materials employed as plasma substitutes. In many respects this is a comparatively new field and agreement on conventions has yet to be reached. For example, the molecular weight of a preparation may be expressed in several ways as an average of the weights of the molecules present, or "weight average molecular weight"; or as an average of the numbers of molecules of different molecular weights present, or the "number average molecular weight". For mixtures containing a wide range of molecular weights, the number average molecular weight is considerably lower than the weight average since the small molecules contribute more to the mixture by their number than by their weight. Thus in a mixture of equal numbers of molecules of weight 1,000 and 10,000 the number average weight would be 5,500, although the molecules of 1,000 molecular weight contribute only 9 1 per cent by weight of the total mixture, the weight average molecular weight would be 9,182. A more accurate representation of the components of a mixture can be obtained by expressing the quantities of material within certain ranges of molecular weight as percentages of the whole in an area distribution diagram. Until such data are provided for all available

plasma substitutes, their detailed comparison is open to criticism. Differences in behaviour in regard to urinary excretion, blood concentration and haemodynamic effect depend on the type of material employed, method of manufacture, batch, dose and concentration.

The mode of action of plasma substitutes is not clearly understood. Haemodilution is a constant effect, as shown by reduction in the packed cell volume and in the total plasma-protein concentration. It is uncertain whether the protein changes are due entirely to dilution or whether there is an actual change in the quantity of protein in circulation. Some of the pressor effects which have been observed after dextran and acacia suggest that the favourable response is not due entirely to the volume of fluid injected or to the quantity of material in circulation, but much further work remains to be done on this aspect of the problem.

The most important of the available plasma substitutes are gum acacia, gelatin, polyvinylpyrrolidone and dextran. It can be seen from the structural formulae of these substances that they are all long chains, the result of the polymerization of smaller molecules. Their behaviour depends on their structure and will be modified by even small changes in the repeating pattern. In those of biological origin like dextran, structural differences may be related to the differences in the strain of the polymerizing organism (*Leuconostoc mesenterioides*). In molecules derived by industrial chemical synthesis, small changes in the conditions of manufacture may cause significant alteration in the end-product.

Gum acacia

In 1906 Morawitz introduced gum saline for the replacement of blood in experimental animals. From 1917 onwards, on the suggestion of Bayliss, it was employed as a 6 per cent solution in 0·9 per cent saline on a large scale in the treatment of shock in battle casualties. It is a hydrophilic colloid derived from the natural gum of the acacia thorn. It has the property of forming aggregates of its small molecules which then remain longer in circulation. The selection of raw material and preparation of the solutions is largely empirical, but satisfactory products are available and give excellent clinical results, and gum saline is still widely employed in spite of much adverse criticism. There is no evidence that acacia is metabolized in the body although it is theoretically possible for this to occur; it is known to be stored for long periods and in large quantities in the liver and reticulo-endothelial system, but a similar type of storage has been observed after the infusion of other plasma substitutes. Bollman (1951) found that liver function was unimpaired in dogs 10 years after the administration of very large quantities of acacia, and that the stored acacia had not produced a tissue reaction.

Amberson (1937) in his review of reports on the use of gum saline concluded that retention of gum acacia in the body and circulation was good, 61, 43 and 25 per cent of the injected dose being still in circulation 24, 48 and 72 hours respectively after injection. Hartmann (1951) recovered 25 per cent of the injected material from the urine in the first 24 hours after injection, and 60 per cent in 7 days.

Gelatin

Gelatin also was first introduced during World War I, but its use was limited because of the dangers of antigenicity and difficulties in preparation. It is derived from the bones and skins of cattle and pigs, and in the last 15 years much progress has been made in processing and preparation. As with other substitutes, there is wide variation between different preparations, but up to now even the best gelatin solutions are more rapidly and completely excreted in the urine than is gum. Since there is no proof that gelatin is metabolized in the body, the high rate and degree of urinary excretion suggest that molecular size is on the whole too small for gelatin solutions to have a

prolonged effect on blood volume; this is borne out by clinical experience. This rapid rate of excretion is possibly also the reason why gelatin is not deposited in body tissues to any significant degree. The viscosity and osmotic pressure of a 6 per cent solution are similar to those of plasma. The chief disadvantage of gelatin, however, is that it gels at room temperature and must be heated before being used. This difficulty was partly overcome by the production of oxypolygelatin (OPG) which is derived from gelatin by condensation and oxidation and which gels at 18° C. There is otherwise little difference between this preparation and gelatin. Recently a gelatin preparation which remains fluid even at 4° C. has been prepared from osseous gelatin (Parkins, Perlmutt and Vars, 1952).

Polyvinylpyrrolidone (PVP)

This is a synthetic water-soluble substance developed in Germany and prepared from formaldehyde, acetylene and ammonia. It is usually employed as a 3·5 per cent solution in a mixture of minerals in the same concentrations as those in which they are found in the blood. It is also known as Periston, kollidon or Plasmosan. It was first employed as a plasma substitute by Hecht and Weese in 1943; the molecular weights of their material ranged from 10,000 to 50,000, with a weight average of 25,000. In spite of this low molecular weight of the material, only 50 per cent of the dose was recovered in the urine (Ammon and Braunschmidt, 1949) More recently, however, recoveries of up to 75 per cent have been obtained (Wilkinson and Storey, 1951, 1952), up to 50 per cent being excreted in the first 24 hours after infusion; measurement of serum concentrations has not been satisfactory Clinical observations suggest that PVP is not as effective as 6 per cent gum acacia in saline or 6 per cent dextran solutions in the treatment of low blood volume states.

Dextran

Dextran is a long-chain polysaccharide composed of glucose molecules joined in a branched chain of two different types of linkage. It is formed by the action of the bacterium *Leuconostoc mesenteroides* in decaying vegetable matter. Natural high polymer dextran forms ropy masses of slime and has been a nuisance in the sugar-beet industry for many years; it was known to Pasteur. In 1937 Stacey suggested that by reason of its molecular structure, dextran might be useful as a substitute for plasma similar to gum acacia. In 1941 Grönwall and Ingelman also suggested that dextran would be of value as a plasma substitute and undertook the necessary hydrolysis and fractionation to reduce molecular size to within safe limits (Ingelman, 1949; Grönwall, 1949). It was subjected to extensive clinical trials in Sweden (Bohmannson and his colleagues, 1946, Thorsen, 1949) and elsewhere (Bull, J. P , and his colleagues, 1949), and subsequently adopted as a routine plasma substitute. During the past six years the methods of preparation of dextran have been improved and clinical and laboratory trials of different types of narrow range molecular fractions have supported the theoretical prediction that prolonged maintenance of a high blood concentration depends on molecular size. Following the injection into normal control subjects of 500 or 1,000 millilitres of a narrowly fractionated preparation, the area distribution diagram of which is shown in Fig 66, only 10 per cent of the dose injected was recovered from the urine after 24 hours, and 15 per cent after 48 hours. At the same time more than 70 per cent of the material injected remained in circulation at 24 hours, and 30 per cent after five days (Wilkinson and Storey, 1951, 1952). The original Swedish preparation from which the most recent fractions have been evolved is shown in Fig. 67; with this preparation about 35 per cent of the injected dose was lost in the urine during the first 24 hours and only 25 per cent remained in circulation. The clinical effects of the most recent narrowly fractionated high molecular weight dextran are thus more prolonged than those of the earlier preparations, and are achieved with

small volumes of the preparation. This preparation is a considerable advance in the development of plasma substitutes.

It is believed that dextran is metabolized to some extent in the human body, but comparatively little evidence has so far been obtained in support of this belief. As with other macromolecules, the injection of large dextran molecules leads to deposition of some of these in the liver, kidney and lymph glands, giving rise to the characteristic foam-cell appearance. These changes are rarely found after injection of the more recent preparations. Functional disturbances of the liver or kidneys have not been encountered. All macromolecules interfere to some extent with blood grouping, and a blood sample for compatibility tests should always be withdrawn before a plasma substitute is injected; if this is not done, blood grouping can still be carried out, but extra care is required in the interpretation of the results.

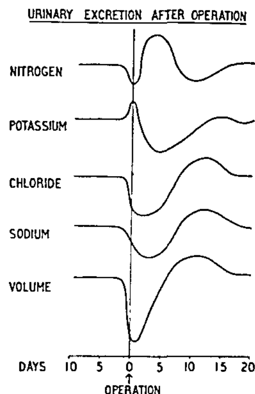


FIG. 65.

Reactions to the infusion of dextran preparations are rare; in Sweden, Thorsen (1949) found an incidence of only 0·8 per cent after 14,000 infusions, compared with 8·2 per cent for whole-blood transfusion during the same period. In normal subjects with normal blood volumes, reactions are very common after dextran infusions (Thorsen, 1952; Evans, 1952), especially with preparations of which a larger proportion is retained within the circulation, and are more common after infusions of 1,000 millilitres than of 500 millilitres. It has been generally assumed that these reactions are of an allergic nature. However, recent experiments in normal subjects suggest that these reactions may be related to the circulatory overloading which follows the rapid injection of narrow fraction dextran solutions into subjects with normal blood volumes (Wilkinson, 1952).

Personal experience in clinical trials of nearly 1,000 units of gum acacia, dextran and polyvinylpyrrolidone indicates that narrowly fractionated dextran of the type indicated in Fig. 66, although similar in initial effect to gum acacia, produces a more lasting effect than either gum acacia or PVP as Plasmosan. These three substances each have potential value, but the choice will ultimately fall on the material which produces the most lasting effect at the lowest cost. At present dextran of the type shown in Fig. 66 is the most efficient and lasting plasma substitute which is available, and is cheaper than either blood or plasma. This fluid represents at least a good preliminary answer to the problem of optimal range of molecular size and to the technical difficulties of hydrolysis and fractionation.

To produce the optimal effect on blood volume, a plasma substitute should be injected rapidly; initially only as much as is necessary to raise the blood pressure to within normal limits should be given; maintenance doses should be given at a fast rate as they are required. It is a mistake to give maintenance infusions as a slow drip, especially if the preparation is not highly fractionated, because the small molecules are excreted in the urine as fast as they are injected, while the largest molecules accumulate in undesirably large numbers. The intravenous infusion should rather be kept running

slowly with glucose solution until there is no longer any need for supplementary replacements.

Because of the haemodilution which is produced, the administration of large volumes of plasma substitutes may be followed by marked anaemia. Towards the end of the first week after severe injury there appears to be a destruction of red cells which is connected in an, as yet, unexplained fashion with the injury. For both these reasons, the administration of whole blood as a supplement to the use of plasma substitutes should be constantly kept in mind. Probably the widest use will be made of plasma substitutes in the treatment of burns. Rosenquist and Thorsen (1951) showed that even the earlier Swedish preparation of dextran was an adequate replace-

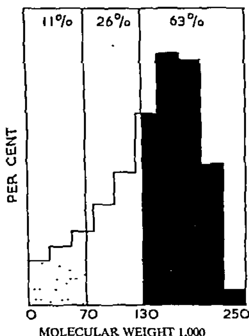


FIG 66.—Area distribution diagram of narrowly fractionated preparation of dextran, showing percentage of total material within three different ranges of molecular weight.

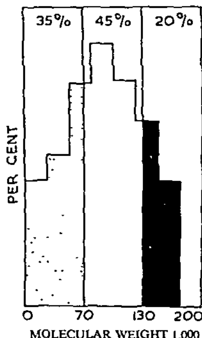


FIG 67.—Area distribution diagram of early Swedish type of preparation of dextran, showing distribution of molecular weight of particles.

ment for the plasma lost in burns, especially when blood also was administered:

used in the treatment of extensive burns with very good results (Wilson, MacGregor and Stewart, 1938). Plasma substitutes are also of value to supplement blood transfusion and so to reduce the requirements of blood. They can be used to replace blood transfusion when the volume required does not exceed one litre, and are useful for starting blood-volume replacement during the interval while compatibility tests are being carried out.

Provision of water

When oral intake has been stopped, sufficient 5 per cent glucose solution should be administered to supply the minimum requirements for insensible water loss and urine formation of at least 1,500 millilitres per day. As has been indicated earlier,

after surgical operations intravenous administration of glucose solution is not without danger, especially in oliguric or anuric patients; when the urine volume remains small in spite of an adequate intake of water, the danger of water intoxication makes curtailment of water intake essential. Solutions containing sodium salts are not of value in the provision of water for normal metabolic requirements at any time, and should be used only for the replacement of sodium losses or deficits. Isotonic glucose solutions may be given by subcutaneous injection, provided some agent which accelerates absorption, such as hyaluronidase, is added.

The difficulty in relieving the thirst which follows accidental injury or surgical operations is not yet sufficiently recognized; only temporary alleviation follows the sucking of moistened gauze, mouth washes or even sips of water, and no greater relief follows the free consumption of water or any other fluid or any type of intravenous infusion. The only exception is in the case of severe reduction of blood volume when rapid adequate replacement of the lost blood or plasma is usually accompanied by reduction in the intensity of the sensation of thirst.

Replacement and maintenance of electrolytes (Table V)

Isotonic saline

Sodium chloride, 0 9 per cent, contains the principal ions, sodium and chloride, of extracellular fluid, and an excess of chloride over sodium. It is used for the rapid replacement of acute losses of extracellular fluid or intestinal secretion.

Saline lactate

The addition of 50 millilitres of molar sodium lactate solution to each litre of isotonic saline makes saline resemble extracellular fluid more closely by increasing the sodium and decreasing the chloride content.

Darrow's solution

Darrow has developed a solution containing 2·7 grammes of potassium chloride in addition to 4 grammes of sodium chloride and 50 millilitres of molar sodium lactate per litre, which he calls "K lactate" and others call "Darrow's solution". The concentrations of sodium lactate and chloride resemble extracellular fluid, and although the potassium concentration is seven times that of serum, it is low enough not to cause toxic potassium concentrations even when given so fast as to provide adequate quantities of sodium and chloride. This solution was introduced for the treatment of acidosis due to sodium and potassium loss in infantile gastro-enteritis with vomiting and diarrhoea.

Potassium chloride is used in the treatment of potassium deficiency with alkalosis due to prolonged vomiting; to 500 millilitres of a 5 per cent glucose solution, 20 millilitres of a sterile 10 per cent solution of potassium chloride are added to make a solution containing 4 grammes of potassium chloride per litre; 500 millilitres of this solution are given by intravenous infusion over a period of four hours. Following this, 500 millilitres of a mixture containing 6 grammes of sodium chloride and 2·7 grammes [illegible] excreted in the urine. The quantities of ammonium chloride which can be employed are limited and it seems wiser to avoid the administration of ammonium when renal function may be impaired by severe alkalosis. The use of ammonium chloride diverts the therapeutic emphasis to the chloride deficiency and bicarbonate excess when the lethal factor is the accompanying potassium depletion.

Sodium chloride may be consumed as half strength (0 45 per cent) saline. *Potassium chloride* has a very unpleasant taste and is best taken as 20 millilitres of a 10 per cent

solution; it should be mixed with an equal quantity of strong fruit juice and well iced before consumption. *Potassium citrate* should also be taken as a medicine; it is usually made up as 30 grains to the ounce, or 2 grammes in 30 millilitres, and should be iced before consumption.

TABLE V

COMPOSITION OF REPLACEMENT FLUIDS

	Na mEq/l	K mEq/l	Cl mEq/l.	HCO_3 mEq/l	Lactate mEq/l
Extracellular fluid	145	5	105	27	—
0·9% sodium chloride (9 g. NaCl/litre)	153	—	153	—	—
Saline lactate (9 g NaCl, 50 ml. molar Na lactate/litre)	203	—	153	—	50
Darrow's solution (4 g NaCl, 2·7 g KCl, 50 ml molar Na lactate/litre)	118	35	103	—	50
0·4% potassium chloride (4 g. KCl/litre)	—	52	52	—	—
Sodium and potassium chloride (6 g. NaCl, 2·7 g KCl/litre)	102	35	137	—	—

The maintenance of nutrition

Parenteral feeding is of limited scope and value since it is confined to the administration of glucose, protein hydrolysate and vitamins. Reference has already been made (page 96) to the protein-sparing effect of 100 grammes of glucose in the starving individual. The value of parenteral protein hydrolysate is limited by the supply of calories as glucose solution which is practicable. It is now well established that before nitrogen equilibrium can be achieved, at least 30 calories per kilogram of body-weight per day must be provided, apart from any protein. In a 60-kilogram adult this implies the provision of at least 1,800 calories in addition to 60 grammes of protein per 24-hour period. To supply 1,800 calories as 5 per cent glucose solution would require the injection of 8·2 litres of solution (3·75 calories per gramme of glucose (McCance and Widdowson, 1946)). A 10 per cent solution of glucose reduces the volume of water required, but increases the incidence of phlebitis; the quantity of glucose lost in the urine increases with the concentration of the infusion and the rate of injection. To overcome these difficulties in the supply of calories, invert sugar and ethyl alcohol have been employed, but their value is as yet uncertain. The best solution lies in the use of fat as the source of calories, but a satisfactory fat emulsion with a reasonably long "shelf-life" has not yet been made.

In spite of these disadvantages, the administration of protein hydrolysates may be of value in some circumstances. In ulcerative colitis, when an intestinal fistula has been present for several weeks, or after prolonged starvation from other causes, the resumption of oral intake is sometimes helped by the repeated intravenous administration of small quantities of protein hydrolysate and glucose (1 litre per 24 hours; 5 per cent amino acids and 5 per cent glucose). Some work of Magee (1945) suggests that this may be related
secondary to prolonged m
to be promoted by the in
administration of protein hydrolysates during the immediate post-operative period is of no nutritional value.

Jejunostomy

This method of feeding is only seldom employed, yet in patients with gastric or duodenal fistulae or oesophageal obstruction its early adoption seems to offer the easiest means of maintaining calorie and protein intake; until a safe and reliable fat emulsion is evolved no other means of provision of calories is likely to be as successful as jejunostomy. There is a good deal of prejudice against the method. In cases of oesophageal obstruction a somewhat lower loop than usual should be used for the jejunostomy so as not to interfere with the choice of jejunum for anastomosis with the oesophagus. Cramps and diarrhoea are said to be severe during the first few days of jejunostomy feeding; these can be avoided provided that strongly hypertonic fluids are not employed in feeding (Allen and Welch, 1941). Difficulty in obtaining and making up some of the complicated, almost galenical, formulae (Hollander's mixture, 12 ingredients; Ivy's mixture, 13 ingredients) is a real handicap, but can be avoided by the use of a simple mixture of whole milk, lactose and dried skimmed milk powder with the addition of vitamin supplements. It is difficult to provide an adequate caloric intake with whole milk alone. Feeds containing a large quantity of fat should be avoided because the jejunum is intolerant of fat. There is no need to use protein hydrolysates in jejunal feeding.

A Witzel type of jejunostomy serves well and may be made under local anaesthesia. The first feed of 120 millilitres of 5 per cent glucose solution should be injected as soon as the operation has been completed, and thereafter two-hourly feeds are given. At first 60 millilitres of milk mixture, followed by 60 millilitres of 5 per cent glucose solution or water are run in from a funnel under gravity. After 12 or 24 hours it is usually possible to increase the quantities to 90 millilitres and then to 120 millilitres of milk mixture, followed on each occasion by an equal volume of water or glucose solution. A total daily intake of 2,400 calories including 120 grammes of protein, 1·76 grammes (76 mEq.) of sodium, 4·48 grammes (116 mEq.) of potassium and 3·38 grammes (90 mEq.) of chloride is provided by a mixture containing 2 pints of fresh whole milk, 240 grammes of lactose, 200 grammes of dried skimmed milk powder. This mixture should be made in the cold by the addition of the lactose and dried milk to the whole milk. After this has been stirred, the supernatant milk is poured off and sufficient water is added to dissolve the sediment; this solution is then mixed with the milk and the mixture kept in a refrigerator until used. The feeds should be warmed before administration to prevent intestinal spasm and deposition of sediment in the tube. Vitamins should be added if jejunostomy feeding is continued for more than a week.

Fluid collected from fistulae or by gastric aspiration can be run into the jejunostomy in the intervals between feeds; when this is done, to reduce the risk of blockage the tube should be washed clean with water before the milk mixture is run in. Potassium chloride can be added to the milk mixture in quantities up to 6 grammes per day, but the addition of even small quantities of sodium chloride is liable to cause diarrhoea.

(*See also British Surgical Practice*. Acidosis, Vol. 1, page 53, S. Key 7.)

REFERENCES

Adolph, E. F. (1947). *The Physiology of Man in the Desert*. New York; Interscience Publishers Inc.
Allen, A. W., and Welch, C. E. (1941). *Surgery*, 9, 163.
Amberson, W. R. (1937). *Biol. Rev.*, 12, 48.
Ammon, R., and Braunschmidt, G. (1949) *Biochem Z.*, 319, 370
[illegible] Edholm, O. G., McMichael, J., and Sharpey-Schafer, E. P. (1944) *Lancet*, 1, 489.
[illegible] 196.
[illegible] mans Green
[illegible] *ch'r. scand.*, 94, 14[illegible]
[illegible]

Bollman, J. L. (1951). *Arch. Surg.*, 63, 749.
Borst, J. G. G. (1948) *Lancet*, 1, 824.
Butterworth
W D'A , Spooner, S J L., Mollison, P. L., and
Paterson, J. C. S. (1949). *Lancet*, 1, [illegible]
— Joekes, A. M , and Lowe, K. G. (1949). *Lancet*, 2, 229.
— — — (1950). *Clin. Sci* , 9, 379.
420
Darrow, D. C (1952). *J. clin. Invest.*,
31, 798.
Darmady, E. M (1952). *Proc R Soc Med.*, 45, 844
Darrow, D C. (1945) *New Engl J. Med* , 233, 91
Dubois, E. F. (1927). *Basal Metabolism in Health and Disease* Philadelphia; Lea and Febiger.
42, 634.
Grant, R. T., and Reeve, E. B. (1941). *Brit. med. J* , 2, 293, 329
Grönwall, A. (1949). *Ugeskr Laeg.*, 111, 1203
W. J. (1949) *Ned Tijdschr. Geneesk* ,
93, 2386.
Labby, D. H., and Hoagland, C. L (1947) *J. clin Invest* , 26, 343
Lucke, B (1946) *Milit Surg* , 99, 371.
McArdle, B , and Merton, P. A (1952). *J Physiol.*, 116, 51*P*
McCance, R. A. (1951). *Medical Research Council Special Report Series*, No. 275, p 21
— and Widdowson, E. M. (1946) *Ibid*, No. 235
— — (1951). *Proc. R Soc B* , 138, 115
McMichael, J , Sharpey-Schafer, E. P , Mollison, P L., and Vaughan, J. M (1943) *Lancet*, 1, 637.
Magee, H E (1945) *Proc R. Soc Med* , 38, 388
Moulton, C R (1923) *J. biol Chem.*, 57, 79
Nadler, C. S , Bellet, S , and Lanning, M. (1948). *Amer J Med.*, 5, 838
Parkins, W M , Perlmutt, J H , and Vars, H. M (1952) *Fed Proc* , 11, 116
Peters, J P (1948) *Surgery*, 24, 568
Rosenquist, H , and Thorsen, G (1951) *Arch Surg* , 62, 524
Schroeder, H. A (1949) *J Amer. med. Ass.*, 141, 117
Sharpey-Schafer, E P (1944). *Clin. Sci.*, 5, 125
de Takats, G (1931) *Amer J. Surg.*, 11, 39
Thorsen, G (1949) *Lancet*, 1, 132.
— (1952) Personal communication
Webster, D R , Henrikson, H. W , and Currie, D J (1950) *Trans. Amer surg. Ass* , 68, 458.
Widdowson, E. M , McCance, R. A., and Spray, C M (1951). *Clin Sci* , 10, 113
Wilkinson, A. W. (1951) *J int Chir.*, 11, 186
— (1952). Unpublished observations.
— and Storey, I D. E. (1951, 1952) Unpublished observations
Wilson, W. C., MacGregor, A. R., and Stewart, C. P (1938) *Brit J Surg* , 25, 826
Zimmermann, B , and Wangensteen, O H (1952). *Surgery*, 31, 654

SURGICAL ASPECTS OF MENINGITIS

By R. T. JOHNSON, O.B.E., F.R.C.S.
Neurosurgeon-in-Charge of the University Department of Neurosurgery, Manchester Royal Infirmary

INTRODUCTION

Progress in the treatment of meningitis embracing the use of new antibiotics, effective against a wider range of organisms, the better use of the older antibiotics, and the earlier diagnosis of the disease, has resulted in a much lower mortality rate. Increasing survival, however, has not led, as it did when antisera and sulphonamide drugs were first used, to an increase in the number of cases with severe and disabling complications, but has been associated with a greatly reduced morbidity. Thus better control of the acute infection has not widened the field of surgery directed to the alleviation of complications, but has enhanced the importance of the search for and the treatment of the primary focus. Such a focus may be one of a wide variety of lesions, not all of them easily recognized, and is very likely to be present when meningeal invasion is by certain organisms or if the infection is recurrent.

ACUTE PYOGENIC MENINGITIS

Although this may be an entity, the meninges alone of the tissues failing to resist invasion during a transient bacteraemia, it is for the most part but the acute spread of an infective process to the subarachnoid pathways. Nevertheless, it is on the management of this episode that the whole course of the disease depends. Acute meningitis must be given the priority of a surgical emergency. Immediately the diagnosis is made, a guess, inspired by a knowledge of the probabilities, must be hazarded as to the causal organism, and optimal treatment instituted at the earliest moment: identification of the organism by culture will render later treatment more exact. Meanwhile consideration must be given to the primary focus and a decision taken on the optimal time for its treatment.

Diagnosis

The ease with which a diagnosis may be established varies with the mode of onset (*see also* Alexander, 1949). There will be no difficulty when the illness commences with the rapid development of headache, confusion, stiff neck and pyrexia, but the diagnostic powers of the ablest clinician may well be tested in the elucidation of such [illegible] careful questioning of the relatives may disclose the [illegible] primary focus, such as recent pain in a chronic discharging ear, a productive cough or a boil.

Acute diffuse epidural spinal abscess may be mistaken for meningitis and may be accompanied by meningitis, but if not so complicated, the importance of diagnosis is increased by the danger of performing lumbar puncture through an infected field. A staphylococcal skin lesion, especially a boil, too often fondly squeezed by a well-wisher, followed by severe and relentless pain in the back and some degree of stiff

neck, will suggest an extradural abscess; confirmation may be found in local spinal tenderness with surrounding oedema and evidence of early cord compression. Difficulties of diagnosis are illustrated by the following case.

CASE I.—M R. Diffuse extradural spinal abscess: meningitis.—Ten days before admission to hospital, an underweight 8-year-old gipsy girl complained of a pain in the middle of her back; a pain which became steadily more severe, and was accompanied the following day by headache, vomiting, fever and drowsiness Five days later she was ill and had retention of urine, but the pain was less noticeable. When first examined, there was no tenderness in the back, but she had all the signs of meningitis, and lumbar puncture revealed a turbid yellow fluid Next day she was worse (temperature 104° F., pulse 140) and pus was aspirated from the lumbar-puncture needle. Culture of the original fluid had now produced a heavy growth of *Staphylococcus aureus* sensitive to all antibiotics. She was given penicillin injections, intrathecal and intramuscular, and aureomycin by mouth. Next day the temperature and pulse rate were lower, but it was noticed that the knee jerks were absent, and that sensation in the legs was impaired. At this stage (15 days after onset) she was transferred for neurosurgical treatment as *a case of unresolved staphylococcal meningitis—with a suspicion that an epidural abscess might be the primary focus.* On admission 24 hours later she was quadriplegic, there was tenderness and oedema over all spinous processes, cervical to lumbar, and there was a fluctuant swelling in the right loin. The diagnosis was now clear and an epidural abscess extending from the foramen magnum to the sacral sac was drained through a small laminectomy opposite the presenting abscess. tubes were placed in the cavity for the subsequent instillation of penicillin She made an uneventful recovery and later admitted to a boil on the buttock 2 weeks before the onset of the back pain

Comment.—In retrospect it was clear that although the child had meningitis on admission, the first lumbar puncture was made across an extradural abscess and the second into the abscess cavity

The presence of neurological signs and the aspiration of pus by lumbar puncture, however, is not unequivocal evidence of an extradural abscess, it may be loculated meningitis, as the following case shows.

CASE II—M F. Otogenic meningitis, spinal loculation abscesses—A woman, 40 years of age, had suffered from a discharging right ear for years. Four months before admission she had had earache for a few days, and 6 weeks before, there had been a transient right facial palsy During the week prior to admission she had become ill; shivering attacks, stiffness of her neck and pain down both legs were prominent from the outset; later she complained of severe headache which prevented her from sleeping One night towards the end of this time she was noticed to be rambling in her speech, and the next morning her husband found her unconscious in bed She was admitted to a local hospital where she was found to have a rigid neck and positive Kernig's sign; it was also noticed that all the tendon reflexes in the right leg were diminished. Lumbar puncture produced a grossly turbid fluid containing in the smear Gram-negative pleomorphic bacilli She was given full doses of sulphadiazine intramuscularly and streptomycin intrathecally and intramuscularly Next day she was conscious and able to drink, but the right leg was now very definitely weak She remained in this state for 48 hours, but then her temperature rose again (103° F), and the right leg became completely paralysed. Lumbar puncture was repeated and at first pus was aspirated through the needle, but when the needle was [illegible]

flaccid paralysis of the right leg in the presence of a completely normal left leg, it was considered to be most unlikely that she had an extradural abscess, and that loculation in the spinal theca was more probable Lumbar puncture produced only a few drops of turbid fluid and the Queckenstedt test showed that there was a complete block Cisternal puncture produced a turbid fluid, but no organisms grew on culture. Gram-negative pleomorphic organisms seen on the first smear of the cerebrospinal fluid which unfortunately was not cultured, and proteus cultured from the ear (sensitive to streptomycin),

provided the only evidence as to the infecting organism which was assumed to be proteus sensitive to streptomycin; so this drug (chloramphenicol was not then available) was given by lumbar, cisternal and ventricular routes. Large doses of Sulphamezathine were also given and she gradually improved; there was also some recovery in the paralysed leg. Eventually, 18 days after the onset, the ventricular and cisternal fluids became clear,

...covered in pus and there were several discrete intrathecal abscesses (Fig. 68). It is of interest that immediately around the sites (Fig. 68, A and E) of injection of streptomycin, the subarachnoid space was relatively clear.

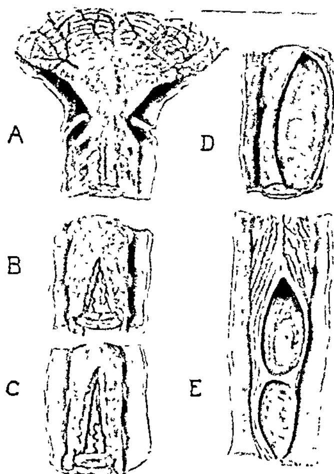


Fig. 68.—Meningitis (*B. proteus*): cerebellum, spinal cord and meninges *post mortem* (*see Case II*). *A*. Cisterna magna; subarachnoid space clear. *B*. and *C*. Lower cervical and dorsal cord; subarachnoid space filled by organizing purulent exudate. *D*. Conus; localized abscess cavity (empty) to right of midline. *E*. Sacral sac, two discrete abscess cavities (empty) lying amongst the cauda equina which are relatively uninvolved.

Comment.—Although this case is described at this juncture to demonstrate the significance of the discovery of pus by lumbar puncture, it illustrates the production of local palsies by loculation, which sometimes occurs at a very early stage in the disease.

Lumbar puncture

Lumbar puncture, essential for diagnosis, is used frequently as a means of introducing antibiotics, and, perhaps not least important, it affords the most accurate gauge of the progress of the disease. Puncture must be made with circumspection where extradural abscess is a possibility. Skill in knowing where the point of the needle lies, and aspiration as the needle is advanced, may enable an extradural abscess to be tapped and so diagnosed before the dura has been breached and infection spread to the meninges. On occasions, lumbar puncture cannot be carried out without anxiety, for example: (1) when brain abscess is producing acute compression and the

signs of meningitis may be accentuated by pressure cone formation—in such cases the abscess should be treated first; or (2) when loss of consciousness rapidly follows the onset of an illness which may indeed be meningitis or could possibly be a surface clot, for both may complicate a head injury within a few hours. Where doubt exists it is advisable to make a burr hole and tap the ventricle; if the loss of consciousness is a result of meningeal infection, the fluid will be unmistakably turbid.

Cerebrospinal fluid

It is essential that no effort be spared in ensuring that the cerebrospinal fluid is examined and set up in culture immediately after puncture, in fact "whilst still hot"; delays and cooling of the fluid will result in an increase in the number of cases of "sterile" meningitis. The success or otherwise of treatment may depend on the accuracy of examination of the first specimen of cerebrospinal fluid, for from that specimen alone may it be possible to grow organisms, and when no organisms can be grown, therapy is blind and fumbling. In this, the closest liaison must be maintained

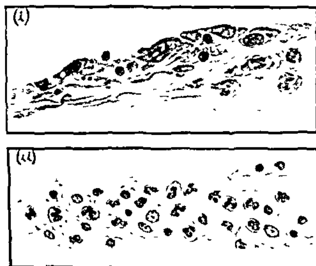


Fig. 69.—Meningitis. subarachnoid space (× 600) (i) *E. coli* (chronic) Subarachnoid space packed with compound granular cells (ii) Pneumococcal (acute) Subarachnoid space packed with polymorphonuclear leucocytes

with the laboratory. The routine here is to inoculate blood agar plates and culture them aerobically, anaerobically and micro-aerophilically; cultures are also made in Brewer's thioglycollate medium, glucose broth and Hartley's broth A considerable number of organisms from deep infections will only grow anaerobically or micro-aerophilically, and will be missed if this technique is not used (Fairbrother, Martyn and Parker, 1951).

Cells.—Turbidity will be present if there are 1,000 cells or more and some degree may be recognizable when there are more than 500 cells. It is important to count the cells—erythrocytes, polymorphs and lymphocytes—and to note any unusual cells, for example compound granular cells may be present in large profusion in chronic low-grade, but nevertheless fatal, infection by *Escherichia coli* (Fig. 69), and tumour cells may be recognized in carcinomatous meningitis. Sometimes meningitis, especially if the organism is *E. coli*, is accompanied by subarachnoid bleeding, and the erythrocyte count may be more reliable than the leucocyte count as a gauge of progress

Smear.—Stained smears m[illegible] morphology alone, may sugg[illegible] of culture together with the [illegible]

Protein —If the protein content is high it is suggestive of a chronic infection, especially

provided the only evidence as to the infecting organism which was assumed to be proteus sensitive to streptomycin; so this drug (chloramphenicol was not then available) was given by lumbar, cisternal and ventricular routes. Large doses of Sulphamezathine were also given and she gradually improved; there was also some recovery in the paralysed leg. Eventually, 18 days after the onset, the ventricular and cisternal fluids became clear, (analysis showed 18 polymorphs, and the protein, which had been 320 milligrams per cent, was less than 85 milligrams, but there was a complete lumbar block and an increasing spastic paraparesis. Three days later there was an acute exacerbation of meningitis and she died. *Post mortem* the ventricles and basal cisterns were clear, but the [illegible] [illegible] space was relatively clear.

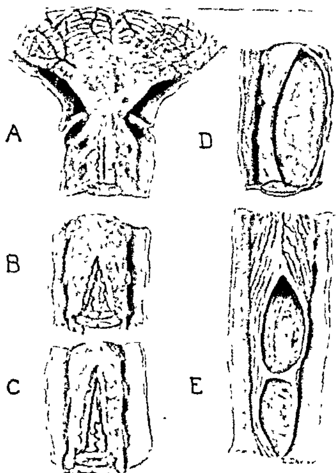


Fig. 68.—Meningitis (*B. proteus*): cerebellum, spinal cord and meninges *post mortem* (*see Case II*). *A.* Cisterna magna; subarachnoid space clear. *B.* and *C.* Lower cervical and dorsal cord; subarachnoid space filled by organizing purulent exudate. *D.* Conus; focalized abscess cavity (empty) to right of midline. *E.* Sacral sac, two discrete abscess cavities (empty) lying amongst the cauda equina which are relatively uninvolved.

Comment.—Although this case is described at this juncture to demonstrate the significance of the discovery of pus by lumbar puncture, it illustrates the production of local palsies by loculation, which sometimes occurs at a very early stage in the disease.

Lumbar puncture

Lumbar puncture, essential for diagnosis, is used frequently as a means of introducing antibiotics, and, perhaps not least important, it affords the most accurate gauge of the progress of the disease. Puncture must be made with circumspection where extradural abscess is a possibility. Skill in knowing where the point of the needle lies, and aspiration as the needle is advanced, may enable an extradural abscess to be tapped and so diagnosed before the dura has been breached and infection spread to the meninges. On occasions, lumbar puncture cannot be carried out without anxiety, for example: (1) when brain abscess is producing acute compression and the

signs of meningitis may be accentuated by pressure cone formation—in such cases the abscess should be treated first; or (2) when loss of consciousness rapidly follows the onset of an illness which may indeed be meningitis or could possibly be a surface clot, for both may complicate a head injury within a few hours. Where doubt exists it is advisable to make a burr hole and tap the ventricle; if the loss of consciousness is a result of meningeal infection, the fluid will be unmistakably turbid.

Cerebrospinal fluid

It is essential that no effort be spared in ensuring that the cerebrospinal fluid is examined and set up in culture immediately after puncture, in fact "whilst still hot"; delays and cooling of the fluid will result in an increase in the number of cases of "sterile" meningitis. The success or otherwise of treatment may depend on the accuracy of examination of the first specimen of cerebrospinal fluid, for from that specimen alone may it be possible to grow organisms, and when no organisms can be grown, therapy is blind and fumbling. In this, the closest liaison must be maintained

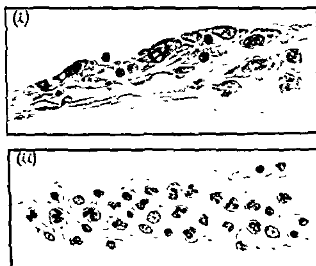


FIG 69.—Meningitis. subarachnoid space (× 600). (i) *E. coli* (chronic). Subarachnoid space packed with compound granular cells (ii) Pneumococcal (acute) Subarachnoid space packed with polymorphonuclear leucocytes

with the laboratory. The routine here is to inoculate blood agar plates and culture them aerobically, anaerobically and micro-aerophilically; cultures are also made in Brewer's thioglycollate medium, glucose broth and Hartley's broth. A considerable number of organisms from deep infections will only grow anaerobically or micro-aerophilically, and will be missed if this technique is not used (Fairbrother, Martyn and Parker, 1951).

Cells.—Turbidity will be present if there are 1,000 cells or more and some degree may be recognizable when there are more than 500 cells It is important to count the cells—erythrocytes, polymorphs and lymphocytes—and to note any unusual cells, for example compound granular cells may be present in large profusion in chronic low-grade, but nevertheless fatal, infection by *Eschericia coli* (Fig. 69), and tumour cells may be recognized in carcinomatous meningitis. Sometimes meningitis, especially if the organism is *E. coli*, is accompanied by subarachnoid bleeding, and the erythrocyte count may be more reliable than the leucocyte count as a gauge of progress.

Smear.—Stained smears may show organisms which, although not identifiable on morphology alone, may suggest what antibiotic should be employed until the results of culture together with the sensitivities to the available antibiotic are known.

Protein.—If the protein content is high it is suggestive of a chronic infection, especially

[illegible]

Sugar.—The sugar content tends to be low in all infections and may give some indication of progress under treatment, but a normal reading does not exclude infection; moreover, it may be reduced in subarachnoid haemorrhage.

Chlorides.—Chlorides are low in tuberculous meningitis, but a normal reading does not exclude tuberculous infection.

Differential diagnosis

Acute meningism may herald the onset of other conditions—such as poliomyelitis, encephalitis, benign lymphocytic meningitis, tuberculous meningitis and subarachnoid haemorrhage—and these must of course be considered in arriving at a diagnosis. It is not likely, however, that having reviewed the mode of onset, the clinical condition and the existence or otherwise of epidemics, and having compared these with the information which can be gathered by a critical examination of the cerebrospinal fluid, that difficulty will often arise. Where doubt still exists and there is no anxiety about the patient's condition, changes in the clinical state and in the cerebrospinal fluid may be intelligently observed for a few days, when the diagnosis may become apparent. If the patient is gravely ill, however, and there is a possibility of bacterial meningitis, it will be wisest to commence treatment with sulphonamides and to continue administration until the patient is better or the diagnosis proven.

There is, however, a disease which experience shows has been mistaken for meningitis even when observed and investigated under the best conditions. This is the cortical angioma which manifests its existence by producing epileptic seizures often of Jacksonian pattern, frequently followed by a Tod's palsy, or by rupture into the ventricle or the subarachnoid space of some of its thin-walled vessels.

It is well known that subarachnoid blood from any cause (aneurysm, angioma, head injury, operation) may give rise to the signs of meningitis; it is further known that the breakdown products of blood, of which bilirubin is probably the most active, can produce a polymorphonuclear reaction in the cerebrospinal fluid (Jackson, 1949), but it is evident that the cellular reaction to angiomas is quantitatively of a different order. On the one hand, where subarachnoid haemorrhage results from causes other than angiomas, red cells or a yellow supernatant fluid leave little doubt as to the cause of the meningism and the polymorphonuclear reaction; on the other hand, leakage of an angioma may produce a high polymorphonuclear response with little or no evidence of haemorrhage. The angiographic findings in a boy who, 12 years before, had been hurriedly admitted to a well-known fever hospital and confidently diagnosed as meningitis, are shown in Fig. 70. There had been, prior to this, as there have been since, several less severe episodes of meningism. Most striking, however, is the case of a young married woman aged 24 years with a cortical angioma who, on three occasions during the previous 11 years, had been admitted to hospital with aseptic meningitis. The last attack occurred in this hospital when she had all the signs of meningitis and a temperature of 102° F.; an immediate lumbar puncture, which was to have shown a blood-stained fluid, confounded the House Physician by producing a turbid colourless fluid containing 4,800 white blood cells and 150 milligrams per cent of protein, but no red blood cells.

It is not certain what factors are responsible for this phenomenon; it may be: (1) thrombosis of the thin-walled vessels characteristic of the angiomas and perhaps some surrounding infarction and clot, usually in the ventricular wall; (2) the response, perhaps allergic, of slightly but chronically inflamed subarachnoid or ventricular tissues conditioned by repeated small subclinical haemorrhages, to a leakage of greater volume—two facts support this: (*a*) angiomas are known to leak repeatedly over the years in a manner not followed by the aneurysms; (*b*) Jackson has shown that a

ventricular fluid from the thin-walled angiomatous vessels.

Cortical angiomas have been discussed at some length because so commonly in our experience have the episodes of leakage been diagnosed as meningitis, or sunstroke, in the past, and as a result of the perfection of the technique of percutaneous

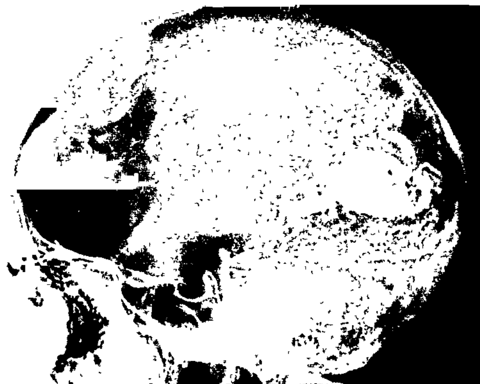


FIG. 70.—Cortical angioma giving rise to "meningitis". Vertebral angiogram demonstrates arteriovenous malformation in the occipital lobe.

angiography they are now easy of diagnosis and not a few can be operated upon and cured

Treatment

The sheet anchor of treatment is full dosage with sulphonamides, adding one or more of the antibiotics as judgment and the result of bacteriological sensitivity tests direct.

General care

To avoid under-emphasis of the importance of the general care of the patient, as opposed to the scientific attack on the invading organism, some aspects of the routine management will be considered first. The patients will need every nursing care, for some are going to be very ill, and they will need to have fluids by whatever route is practicable—mouth, nasal tube or intravenously. Associated disease must be considered and treated according to its relative importance, but special mention must be made of chest complications, especially in unconscious or very drowsy

patients in whom, because of central damage, respirations may be rapid and shallow. Very high dosage of intramuscular penicillin is effective in combating infection, but secretions which the unconscious or ill patient is unable to expectorate must be removed. Modified postural drainage, the foot of the bed uplifted, physiotherapy, breathing exercises and some form of mechanical suction may be life-saving; the lightening of the state of consciousness that sometimes follows these manoeuvres will be a surprise to anyone unfamiliar with the depressant effect of even minor degrees of respiratory embarrassment on cerebral function. Skin will require the usual care, but incontinence, high fever, opisthotonus and rigidities will add to the difficulties. Restlessness may be extreme and must not be assuaged by repeated and increasing doses of phenobarbitone; this is extremely dangerous and can of itself tip the balance against recovery.

Perhaps clinicians are not fully alive to the risks of the barbiturates; toleration of high and prolonged dosage by epileptics who are otherwise well has at times led to its reckless administration to ill and toxic patients who endure it badly, especially when repeated dosage and poor excretion combine to build up a high concentration in the body.

A certain amount of sedation may be advisable, especially in the presence of convulsions which should always arouse a suspicion that the meningitis is not uncomplicated, but the dose should be small and restlessness should be managed by skilled and tolerant nursing; better a few wakeful nights than perilous induced sleep, which will come naturally when the antibiotics have controlled the infection. A full bladder, wet sheets, headache and backache increase restlessness and should not be overlooked, nor should be forgotten the great relief that lumbar puncture may sometimes bring. There has been much criticism of lumbar puncture recently (especially in the United States of America: Hoyne, 1948; Hoyne and Riff, 1951) and antibiotics which find their way into the cerebrospinal fluid in effective concentration when given orally have been heralded not so much for intrinsic merit but for the avoidance of puncture which they permit. However laudable the attempt to obviate a somewhat unpleasant procedure, it remains to be seen if the results are as good; in fact there is already some evidence that this is not so in pneumococcal meningitis (Gibson and James, 1952). Good technique will minimize the hazards of puncture, especially secondary infection.

In order to provide continuous care during the acute phase of the illness one cannot over-emphasize the importance of nurses special to the patient; they may avert a fatality before antibacterial methods have had time to act. Finally, as the fever subsides, the patient returns to consciousness and lucidity, and the cerebrospinal fluid clears, the relief from anxiety thus produced must not permit oversight of the value of physiotherapy in preventing contractures. Apathy and pain militate against voluntary movement, and most severe cases will at this stage show some degree of spasticity, or foot drop, and not a few flexion contractures of the legs.

Specific treatment

The consensus of opinion of those authorities who have had the widest experience and success in treating meningitis is that sulphonamides should be the basis of treatment (Alexander, 1952; Smith, 1951). These drugs have a wide antibacterial [illegible]

being cured by quite a small oral dose before the organism [illegible] the sensitivity to the various antibiotics known. Cases of meningitis coming under surgical care, however, will rarely be mild and uncomplicated; the greater number will be cases secondary to a primary focus or to some surgical manipulation or operation and will require an extensive course of treatment. It is not without personal interest that sulphonamides, although not ideal, should have retained pride of place,

for when penicillin was introduced during World War II as the panacea of infection, especially fatal war wounds of the brain, it failed, in the Eastern theatre, to better the results which had been obtained with high sulphonamide dosage (Johnson and Dick, 1945). The reason was twofold (1) the high incidence of infection with *E. coli*—an organism not regarded in temperate climates at that time as of great virulence or importance, and (2) the low incidence of staphylococcal infections largely resistant to sulphonamides but at that time so sensitive to penicillin.

Chemotherapy.—The aim is to attain the required level of drug in the cerebrospinal fluid at the earliest moment, and to maintain this level until the infection is controlled. We have no definite figures on the requisite sulphonamide level, nor do we know if there is a level above which there is danger and yet no further prospect of success. Experience obtained before antibiotics were available to confuse the issue suggested that a cerebrospinal-fluid level of 20 milligrams per cent was far more effective than 10 milligrams per cent. One of the difficulties of investigation is that sensitivity tests of organisms to various concentrations *in vitro* do not always bear out the findings *in vivo*, where the drug would appear to be relatively more effective. Various drugs may be used and probably differ little in their action. We have used Sulphamezathine (Sulphadimidine) and have kept to this because we are familiar with it. In cases where the patient is ill, or where it is anticipated that the illness may be severe, the route of administration should be intravenous; for in addition to the need to administer a "loading" dose directly into the blood stream, there must be no possibility that failure to reach the necessary level results from vomiting or the inability of an ill patient to absorb drugs from the bowel. It is the practice in the Manchester Royal Infirmary to set up an intravenous drip and to add soluble Sulphamezathine to the bottles of glucose-saline solution, adjusting the amount to maintain the desired dosage. Harland and Goodall (quoted by Johnson and Dick, 1945), in some unpublished work on volunteers, found that a dose of 3 grammes of Sulphamezathine given intravenously 4-hourly produced a cerebro-spinal-sulphonamide level of only 10 milligrams per cent at the end of 12 hours, but that if the dose was increased to 6 grammes for the first two 4-hourly doses, the level was 12–16 milligrams in the first 12 hours and 20–30 milligrams in 48 hours, and that once attained, this level could be maintained by 2 grammes 4-hourly. This work makes it quite clear that even with massive intravenous doses, high levels are not attained in the cerebrospinal fluid [illegible] evident within a few hours of attaining an adequate level; or (2) if evidence of toxicity appears.

Renal complications of soluble Sulphamezathine have been extremely rare, even using high dosage: pyrexia and rashes are not uncommon and are of little consequence, but vomiting, if repeated, is a sign of grave omen, especially if accompanied by abdominal distension which should be looked for constantly, for within a short time paralytic ileus may ensue. This complication, which perhaps is connected with the discharge into the bowel of sulphonamide concentrated in the gall-bladder, has been the most serious, and has given cause for most anxiety, in a large series of patients treated personally. Lives have been saved, however, by heroic measures, as the following case illustrates.

CASE III.—J. H. Cerebellar astrocytoma; complete removal; post-operative meningitis.—This patient, a girl of 13 years, had shown the usual mild pyrexia since operation, but was otherwise well until the third post-operative day, when her temperature rose to 103° F. Sulphamezathine was given by mouth (3 grammes followed by 2 grammes, 6-hourly), but there was little response and she became acutely ill on the fifth post-operative day, when

patients in whom, because of central damage, respirations may be rapid and shallow. Very high dosage of intramuscular penicillin is effective in combating infection, but secretions which the unconscious or ill patient is unable to expectorate must be removed. Modified postural drainage, the foot of the bed uplifted, physiotherapy, breathing exercises and some form of mechanical suction may be life-saving; the lightening of the state of consciousness that sometimes follows these manoeuvres will be a surprise to anyone unfamiliar with the depressant effect of even minor degrees of respiratory embarrassment on cerebral function. Skin will require the usual care, but incontinence, high fever, opisthotonus and rigidities will add to the difficulties. Restlessness may be extreme and must not be assuaged by repeated and increasing doses of phenobarbitone; this is extremely dangerous and can of itself tip the balance against recovery.

Perhaps clinicians are not fully alive to the risks of the barbiturates; toleration of high and prolonged dosage by epileptics who are otherwise well has at times led to its reckless administration to ill and toxic patients who endure it badly, especially when repeated dosage and poor excretion combine to build up a high concentration in the body.

A certain amount of sedation may be advisable, especially in the presence of convulsions which should always arouse a suspicion that the meningitis is not uncomplicated, but the dose should be small and restlessness should be managed by skilled and tolerant nursing, better a few wakeful nights than perilous induced sleep, which will come naturally when the antibiotics have controlled the infection. A full bladder, wet sheets, headache and backache increase restlessness and should not be overlooked, nor should be forgotten the great relief that lumbar puncture may sometimes bring. There has been much criticism of lumbar puncture recently (especially in the United States of America: Hoyne, 1948; Hoyne and Riff, 1951) and antibiotics which find their way into the cerebrospinal fluid in effective concentration when given orally have been heralded not so much for intrinsic merit but for the avoidance of puncture which they permit. However laudable the attempt to obviate a somewhat unpleasant procedure, it remains to be seen if the results are as good; in fact there is already some evidence that this is not so in pneumococcal meningitis (Gibson and James, 1952). Good technique will minimize the hazards of puncture, especially secondary infection.

In order to provide continuous care during the acute phase of the illness one cannot over-emphasize the importance of nurses special to the patient; they may avert a fatality before antibacterial methods have had time to act. Finally, as the fever subsides, the patient returns to consciousness and lucidity, and the cerebrospinal fluid clears, the relief from anxiety thus produced must not permit oversight of the value of physiotherapy in preventing contractures. Apathy and pain militate against voluntary movement, and most severe cases will at this stage show some degree of spasticity, or foot drop, and not a few flexion contractures of the legs.

Specific treatment

The consensus of opinion of those authorities who have had the widest experience and success in treating meningitis is that sulphonamides should be the basis of treatment (Alexander, 1952; Smith, 1951). These drugs have a wide antibacterial spectrum, which includes the Gram-negative organisms, and are usually most effective in pneumococcal, streptococcal and meningococcal meningitis, many such cases being cured by quite a small oral dose before the organism is identified by culture and the sensitivity to the various antibiotics known. Cases of meningitis coming under surgical care, however, will rarely be mild and uncomplicated; the greater number will be cases secondary to a primary focus or to some surgical manipulation or operation and will require an extensive course of treatment. It is not without personal interest that sulphonamides, although not ideal, should have retained pride of place,

for when penicillin was introduced during World War II as the panacea of infection, especially fatal war wounds of the brain, it failed, in the Eastern theatre, to better the results which had been obtained with high sulphonamide dosage (Johnson and Dick, 1945). The reason was twofold (1) the high incidence of infection with *E. coli*—an organism not regarded in temperate climates at that time as of great virulence or importance, and (2) the low incidence of staphylococcal infections largely resistant to sulphonamides but at that time so sensitive to penicillin.

Chemotherapy.—The aim is to attain the required level of drug in the cerebrospinal fluid at the earliest moment, and to maintain this level until the infection is controlled. We have no definite figures on the requisite sulphonamide level, nor do we know if there is a level above which there is danger and yet no further prospect of success. Experience obtained before antibiotics were available to confuse the issue suggested that a cerebrospinal-fluid level of 20 milligrams per cent was far more effective than 10 milligrams per cent. One of the difficulties of investigation is that sensitivity tests of organisms to various concentrations *in vitro* do not always bear out the findings *in vivo*, where the drug would appear to be relatively more effective. Various drugs may be used and probably differ little in their action. We have used Sulphamezathine (Sulphadimidine) and have kept to this because we are familiar with it. In cases where the patient is ill, or where it is anticipated that the illness may be severe, the route of administration should be intravenous; for in addition to the need to administer a "loading" dose directly into the blood stream, there must be no possibility that failure to reach the necessary level results from vomiting or the inability of an ill patient to absorb drugs from the bowel. It is the practice in the Manchester Royal Infirmary to set up an intravenous drip and to add soluble Sulphamezathine to the bottles of glucose-saline solution, adjusting the amount to maintain the desired dosage. Harland and Goodall (quoted by Johnson and Dick, 1945), in some unpublished work on volunteers, found that a dose of 3 grammes of Sulphamezathine given intravenously 4-hourly produced a cerebro-spinal-sulphonamide level of only 10 milligrams per cent at the end of 12 hours, but that if the dose was increased to 6 grammes for the first two 4-hourly doses, the level was 12–16 milligrams in the first 12 hours and 20–30 milligrams in 48 hours, and that once attained, this level could be maintained by 2 grammes 4-hourly. This work makes it quite clear that even with massive intravenous doses, high levels are [illegible]

evident within a few hours of attaining an adequate level; or (2) if evidence of toxicity appears.

Renal complications of soluble Sulphamezathine have been extremely rare, even using high dosage: pyrexia and rashes are not uncommon and are of little consequence, but vomiting, if repeated, is a sign of grave omen, especially if accompanied by abdominal distension which should be looked for constantly, for within a short time paralytic ileus may ensue. This complication, which perhaps is connected with the discharge into the bowel of sulphonamide concentrated in the gall-bladder, has been the most serious, and has given cause for most anxiety, in a large series of patients treated personally. Lives have been saved, however, by heroic measures, as the following case illustrates.

CASE III.—J. H. Cerebellar astrocytoma; complete removal; post-operative meningitis.—This patient, a girl of 13 years, had shown the usual mild pyrexia since operation, but was [illegible]

Sulphamezathine was given intravenously in glucose-saline at the rate of 4 grammes [illegible] conscious and swallowing, and eventually made a complete recovery, but for weeks she was apathetic, for 2 *months she was incontinent*, and she developed flexion contractures of her legs, which remained spastic for several months. Eventually recovery was complete.

Comment.—At no stage was any organism grown on culture of the cerebrospinal fluid. A *graph showing the* polymorphonuclear response in the cerebrospinal fluid and the sulphonamide levels in blood and cerebrospinal fluid from the third to the fifteenth post-operative day is given in Fig. 71.

Sulphonamide levels 72 hours after a usual oral dose of Sulphamezathine were: blood 20 milligrams per cent and cerebrospinal fluid 7 milligrams per cent, and infection was gaining ground. At this stage intravenous Sulphamezathine in high dosage was commenced and 2 days later the cerebrospinal-fluid level was 40 milligrams per cent. At this time (eighth post-operative day) the child was almost moribund, and it is interesting to note *that the cerebrospinal fluid had become heavily blood-stained, and that the sulphonamide* level was as high as the blood level. From this point, although there was little change in her clinical condition, the cerebrospinal-fluid polymorphs (never very high) began to fall, and the cerebrospinal-fluid sulphonamide level *started to draw away from the blood level.* On the twelfth post-operative day she was conscious, and the cerebrospinal-fluid sulphonamides had now fallen to two-thirds of the bloodl evel. When administration of Sulpha-[illegible] ay at a greater rate [illegible]. It is interesting to [illegible] was virtually non-existent to sulphonamide, and that re-emergence of this barrier was the first indication of recovery.

Since sulphonamides may not attain a bacteriostatic level for 48 hours in spite of high dosage, it may be advantageous to institute treatment by one of the antibiotics from the start, especially if the organism can be forecast by any means; it is unlikely that any harm will come of this and in any case change to an antibiotic will have to be made if the organism proves resistant to sulphonamides. Moreover, there would *appear to be very good evidence for the synergic action of penicillin and sulphon-*amides in pneumococcal meningitis (Waring and Smith, 1944; Smith, Duthie and Cairns, 1946).

Antibiotics.—The number of antibiotics now available makes the selection of those to be used a matter requiring experience and judgment. Furthermore, progress in the study of their characteristics and their mode of action has resulted in a subject of such complexity that it is no easy task to master it. However, anyone treating acute infections must have some understanding of the problem and must be abreast of new developments, *for the choice of the right antibiotic and its use in the right dosage* at the right moment may be the only means of saving life. It is questionable whether the term antibiotic has any meaning now that chloramphenicol has been synthesized, the formulae of penicillin and terramycin are known, and a beginning made in the reduction of antibacterial effect to a series of known or suspected biochemical reactions. It is to be hoped that further clarification of those problems by providing simple answers to the requirements for bacterial growth will end the burden of having to understand the vagaries of an ever-increasing number of empirical antibacterial substances.

One of the great difficulties in therapy is that behaviour *in vitro* is by no means an exact indication of behaviour *in vivo*; the development of resistance, antagonistic or synergic action of antibiotics used together and *the curious finding that resistant* strains may eventually fail to grow, or grow feebly unless supplied with the antibiotic, are, for the most part, findings within the restricted space of the culture plate; there is evidence that some of these phenomena are due to the accumulation of bacterial

metabolites, and would not be repeated in the living host, where resistance occurs less commonly than *in vitro*, and where there is so far little evidence of synergism and less of antagonism when two antibiotics are used together; a notable exception is the increased mortality from pneumococcal meningitis when oral aureomycin (bacteriostatic) is used with intramuscular penicillin (bactericidal) (Lepper and Dowling, 1951). The occurrence of organisms unpredictable and varying in their resistance is the great problem in treatment by antibiotics and has been a stimulus in the search for new substances. Some organisms are naturally resistant, others develop resistance under treatment, and whether this is a process of changing metabolism, or whether it

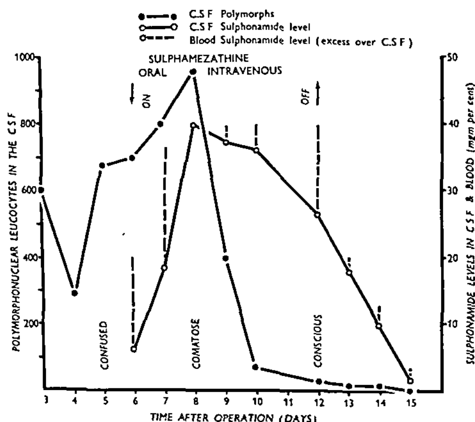


FIG. 71.—Acute meningitis treated with intravenous Sulphamezathine (*Case III*) Graph of C.S.F. leucocytes, and sulphonamide levels in blood and C.S.F. Showing relationship of clinical state, C S F cells and blood-brain barrier.

is by selection (the sensitive strains being killed off and those resistant allowed to multiply), or a combination of the two, is not yet known. A number of facts which are of some help clinically have emerged from this volume of research and the main conclusions may be summarized.

(1) Resistance is highly specific, especially so as regards penicillin and streptomycin, and hence the rationale of employing two antibiotics when the organism is not very sensitive to either, although in practice there is little evidence of the value of this. There may be some cross resistance to the bacteriostatic antibiotics, for example, resistance to aureomycin may be associated with some degree of resistance to chloramphenicol and terramycin

(2) Pneumococci, streptococci and meningococci give little trouble, they are sensitive to all the antibiotics (except polymyxins) and rarely develop resistance.

(3) Staphylococci, apart from resistant strains, are extremely sensitive to penicillin and do not readily develop resistance during the adequate treatment of an acute infection. It must be remembered, however, that in hospital cross infections there is a great increase of resistant strains.

(4) The most effective way of combating resistance is early treatment with the [illegible]

ser [illegible] cally necessary to attain a high local concentration at the commencement of treatment) and to the [illegible]

[illegible] of an antibiotic which can be obtained in the cerebrospinal fluid in good concentration and yet highly sensitive to a second antibiotic which can reach the cerebrospinal fluid only in small amounts, it may be better to treat the patient with the first antibiotic. Another important consideration is that septicaemia and adjacent infection be treated simultaneously; blood cultures are commonly positive in the acute phase, perhaps especially important in meningococcal infection, when suprarenal haemorrhage may produce sudden death (Waterhouse-Friderichsen's syndrome, in which timely administration of cortisone may save some lives). For this reason systemic administration should not be abandoned however effective intrathecal therapy is against the meningitis.

As a guide to therapy the characteristics of the principal antibiotics are given below. Antibiotics for intrathecal use should be aseptically prepared in neutral isotonic solution and single doses, without preservatives, sealed in individual glass ampoules.

Penicillin.—Effective against most of the Gram-positive organisms, soluble in water, giving a neutral solution. Small amounts, greater in meningitis, find their way into the cerebrospinal fluid when given parenterally; new penicillin compounds promise to be more effective in this respect. Given intramuscularly the dosage may be massive. The pure crystalline penicillin is relatively non-irritant and may be injected into the ventricle and spinal theca in small amounts for long periods. Doses greater than 20,000 units have produced seizures and doses of 50,000 and 100,000 units have induced status epilepticus and caused death following ventricular and spinal thecal injection. Extremely high dosage may be safely used in brain-abscess cavities, but the intrathecal dose should not be exceeded in the subdural space. Penicillin is the ideal antibiotic where the organism is sensitive to a level which can readily be attained in the cerebrospinal fluid. Penicillin occasionally produces allergic reactions but is otherwise safe.

Streptomycin.—Effective against *Mycobacterium tuberculosis*, its use against other organisms, including the Gram-negative, which if sensitive may be killed extremely quickly, is restricted by its property of rapidly inducing resistance although it may be useful given in one or two doses initially. Soluble in water to produce a neutral solution. Some finds its way into the cerebrospinal fluid when given parenterally, and more if the meninges are inflamed, streptomycin may be given intrathecally over long periods in doses up to 100 milligrams; it produces a slight reaction. It can produce deafness and vestibular paralysis, but these are less marked with new strains.

Chloramphenicol.—Chloramphenicol is effective against a wide range of organisms, and acts very rapidly. It is soluble in water, producing a neutral solution containing 2 milligrams per millilitre; this may be autoclaved. It is freely diffusible into the cerebrospinal fluid (25 micrograms to 50 micrograms) when given orally. It is also freely diffusible into [illegible]

infected loculus), but 10–14 milligrams is a more usual dose, [illegible]

in treating meningitis caused by *B. proteus*, an organism resistant to most other antibiotics,

Ps. aeruginosa and *E. coli* infections; they are soluble in water, producing a neutral solution; on administration there may be slight irritation in the subarachnoid space (Swift and

They have, however, proved useful given intrathecally in doses of 40,000 units; 100,000 units have been given in a severe case of *B. coli* meningitis and produced drowsiness and coma, but with recovery and cure of the patient. Renal damage is a risk should the polymyxins be given systemically.

Aureomycin.—Aureomycin is effective against a wide range of organisms. It is soluble in water, giving an acid solution (*p*H 2·5); a buffered solution (1 milligram per millilitre) may be introduced intrathecally for short periods in doses of 2·5 milligrams up to 10 milligrams (Ainley-Walker and Bosanquet, 1952). It has a moderately irritant effect and is

drug is withdrawn It is useful for Gram-positive organisms resistant to penicillin, but solutions which require elaborate buffering are not entirely satisfactory for intrathecal use Gastro-intestinal disturbances and fungus infections may result from the administration of aureomycin.

Terramycin.—Effective against a wide range of organisms. It is only slightly soluble in water, giving a slightly acid solution, and more soluble in acid or alkaline solutions. Little finds its way into the cerebrospinal fluid. It promises to be more effective than aureomycin for Gram-negative infection in general, but is of very limited use in meningitis. Its toxic effects are the same as for aureomycin.

Course of the disease

The correct management of meningitis demands a daily, or in the acute stage a twice daily, review of progress and medication Clinical improvement, striking and dramatic, occurring in the first few days may be ample evidence of recovery, but slight or moderate degrees of improvement, especially if delayed, can be misleading, and the withdrawal of specific treatment at this stage will often allow reactivation of dormant infection; an organism difficult to suppress—one that is only slightly sensitive to available drugs—may then be completely out of control. Of our fatal cases of meningitis most have been held in check for a while, but have eventually died because such drugs as we possessed were not quite powerful enough, or the infection was too advanced, or because therapy was either mistakenly, or perforce because of toxic symptoms, withdrawn too soon, and once the organism had escaped there was no way back. The cerebrospinal fluid provides the most accurate indication of progress, and a recorded increase in the cells and protein will warn against a lessening of vigilance and therapy because of clinical improvement. For this reason puncture should be done frequently, daily or twice daily at first, and the fluid examined for

in the presence of a worsening of the clinical condition indicates the need for cisternal or ventricular puncture or both, especially when drugs are being given intrathecally. When the pressure is high and headache severe, much good and relief of pain may follow a reduction of the pressure, it is customary to take the pressure halfway down to normal, provided the dynamics are normal, and there is no evidence of abscess or loculation. A low pressure, especially if associated with the signs of ventriculitis, is of

grave omen, for it means ependymitis and inflammation of the choroid plexus (Johnson, 1947).

Recovery, however, can take place from this stage; it is an indication to increase fluid intake, lower the patient's head if raised, and to increase or vary the chemotherapy. Bleeding into the subarachnoid space has been mentioned above as a possible accompaniment of Gram-negative meningitis. Frank blood may be associated with few white cells, and a reduction in the number of red cells the first sign of control of the infection; the fluid changes in colour from bright red to port wine but is still highly proteinous and turbid; then as the meningitis is cured the fluid becomes straw-coloured and clear. On rare occasions *E. coli* may be present in the cerebrospinal fluid without causing much cellular reaction, and may eventually die out without treatment. It should be noted that polymyxin and chloramphenicol are irritant if used intrathecally and may cause an increase in the white cells; concomitant clinical improvement will dispel any fears that this is a relapse of meningitis. Rising protein in the cerebrospinal fluid may indicate complications, but more commonly is an indication of persistent inflammation by a chronic infection, especially by Gram-negative organisms. Rarely high at first, the protein does not rise *pari passu* with the degree of infection, but in the later stages of chronic disease it rises rapidly to a high level with a mild recrudescence of meningitis; it is the response of inflamed meninges to further slight infection and may not again fall to normal until long after the patient is clinically well.

The cerebrospinal fluid may clear although there is progressive neural damage and deterioration, and then quite suddenly the patient will die within a short time of a final episode of meningitis; the interval may be so short, in fact, that *post mortem* there is little evidence of recent meningitis; a wave of infection spreading from a subarachnoid loculus has quickly proved fatal in the presence of extensive brain damage, the result of chronic infection never completely controlled.

Surgical treatment

Apart from the treatment of a primary focus, surgery has little part to play in acute meningitis. Continuous lumbar or ventricular drainage, introduced by Victor Horsley in a desperate attempt to drain subarachnoid infection as an abscess elsewhere would be drained, are now seldom employed. Prior to the effective treatment of meningitis with antibiotics, high papilloedema not uncommonly developed in the acute phase of the disease, and drainage improved the patient's condition and may have prevented blindness in some instances. Ventricular tubes however carry the risk of introduction of secondary resistant infections (*Pseudomonas aeruginosa* is particularly dangerous in this connexion) and have the disadvantage that it is more difficult to maintain an adequate level of sulphonamide or antibiotic in the cerebrospinal-fluid pathways especially beyond the point of drainage (*vide* post-operative meningitis). Cairns (1949) drew [illegible] to the [illegible] lumbar fluid following continuous ventricular [illegible] tuberculous [illegible] There is no doubt however that, in rare instanc[illegible] or [illegible]ular drainage is useful as a temporary measure t[illegible] the exudates of active infection, for example bl[illegible] of Sylv[illegible] foramina of

1946. Arnold of Boston (1951) reported 4 cases in infants; some of the effusions were clear yellow and others were purulent. The fontanelle should be tapped if there is evidence of local inflammation, failure to improve on adequate therapy after 72 hours, or later convulsions, vomiting and papilloedema. In older children or adults, evidence that all is not well may indicate the desirability of making burr holes. Aspiration and the instillation of antibiotics, drainage and perhaps later excision of a membrane (as in subdural haematoma) may be required.

Certain observations must be made on this erstwhile apparently rare condition.

(1) It was noted in fatal cases of meningitis before treatment was available.

(2) It is more common in some clinics than in others, and more common in infants than adults.

(3) Although lumbar puncture has been incriminated, the incidence of this complication seems to have risen with the advent of drugs which can be given systemically alone.

It is now well known that rupture of the arachnoid commonly occurs in severe subarachnoid haemorrhage, and blood and cerebrospinal fluid escape into the subdural space (Dandy, 1944; Logue, 1951; Bassett and Lemmen, 1952). This may be extensive enough to produce signs, or it may be a finding at operation undertaken to treat the aneurysm or angioma. It would seem likely that high pressure in the subarachnoid space can cause rupture of the arachnoid with the development of a subdural effusion; this is supported by Cairns (Smith, Duthie and Cairns, 1946) who reports a case in which intrathecal penicillin leaked into a subdural hydroma in such quantity that it suggested an arachnoidal tear. Whether these effusions are serous, haemorrhagic or purulent will depend on the stage of the disease at which the rupture occurs, on the local effective level of antibiotic and on the pathological changes in adjacent membranes and blood vessels. It should be remembered that in some cases the meningitis and effusion may have originated from a common surface infection (Spitz and his colleagues, 1946). However, it would be reasonable to suppose that repeated lumbar puncture, by reducing the subarachnoid pressure, far from causing subdural effusions, might tend to prevent them in a certain number of cases.

POST-OPERATIVE MENINGITIS

That the successful outcome of a frequently long and painstaking operation should be marred by post-operative infection resulting in a fatality or severe invalidism, is a tragedy of the first magnitude; there can be no greater disappointment to a surgeon. Invasion by virulent organisms may cause anxiety in any field of surgery, but prompt recognition and adequate treatment should bring early resolution without sequelae. Multiplication of organisms of low virulence (many regarded as saprophytes) may occur in the cerebrospinal fluid, especially where large cavities containing damaged tissue afford an ideal culture medium, and the onset may be insidious and fail to give any cause for alarm until the relentless advance of infection has produced extensive damage from which (even if the infection can be cured) recovery must be slow and incomplete.

Although most commonly encountered following operations on the [illegible]

Following operations on the cranium

Mastoidectomy

Usually the small dural tear will safely heal if the meningitis can be controlled by chemotherapy; it should be remembered that meningitis may remain localized at its point of origin for some time, giving rise to few cells in the cerebrospinal fluid.

Paranasal sinus operations

Removal of polypi may result in cerebrospinal-fluid rhinorrhoea and the ri meningitis. It may be necessary to repair the defect intracranially with fascia.

The dura may be torn whilst operating upon acute purulent sinusitis resulti meningitis, subdural empyema or both. If a subdural empyema is confirmed by hole, a frontal bone flap should be turned and the defect closed by a small pat fascia: this may be the safest procedure in meningitis, where cerebrospinal fluid be in contact with a widely opened and infected sinus, especially if the infe remains uncontrolled by antibiotics after a trial of 24 hours.

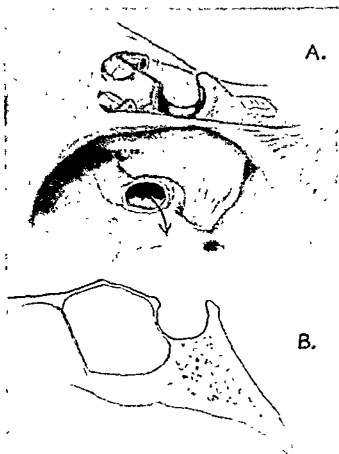


FIG. 72.—Relations of spheno sinus. *A*. Drawing of the pit fossa from the left side. *B*. S section through sphenoidal and pituitary fossa. The sphe sinus bulges into the c chiasmatis between the optic forming the anterior wall pituitary fossa, and may laterally between the fo rotundum and foramen where it is liable to injury in tures of the middle fossa.

Sphenoidal approach to the pituitary

[illegible]
[illegible]
[illegible]
for pituitary capsule and opened (Fig. 72).

Following operations on the spine

Operations for prolapsed disc carry a risk of meningitis if the d[illegible]ura has [illegible] (usually in the crook of a nerve root) or sometimes [illegible]f a punc has been [illegible] nal anaesthesia. Invasion of the meninges is usuall[illegible]y associ [illegible] pers [illegible] ere pain, rising temperature and p[illegible]ulse sh [illegible] wound [illegible] be inspected without delay. Dia[illegible]nostic [illegible] of [illegible] done by the cisternal route or by [illegible] ventric

Following brain operations

Certain features of meningitis following brain operations merit consideration. Infection is not the hazard of the indistinguished in neurosurgery; the biopsy, the root section, the partial removal of a tumour; it is the hazard of the best, the total removal of a solid vermis astrocytoma, the removal of a large meningioma involving several fossae of the skull, the staged removal of a solid angioma involving the roof or side walls of the fourth ventricle. So it is that with an increasing number of survivals from definitive and extensive operations, the higher will be the infective rate: in spite of all precautions and the prophylactic use of sulphonamides and various antibiotics, the risk of infection remains a fear that has not much diminished, although wound infection is now virtually unknown.

Diagnosis

Recognition of the early stages of infection in the post-operative period is not easy, especially where blood spilled into the subarachnoid space is itself producing meningeal inflammation. Careful observation of the patient's condition will often show that all is not well, and that recovery is unduly delayed. In fact, the clinical state is the best guide as to whether infection is present or not. Examination of the cerebrospinal fluid may show initially red cells and perhaps a polymorphonuclear reaction of up to 1,000 cells (and puncture will relieve meningeal reaction to blood), but later as daily punctures are continued, cases of infection will show an increase in cells and an organism may be cultured. It is important to recognize that red cells may be part of an infection and not just the aftermath of operation. A great increase in the cerebrospinal-fluid red cells associated with a rise of temperature to 103° F. occurred 8 days after the removal of a cerebellar haemangioma and is shown graphically in Fig. 73. There was an initial response to Sulphamezathine which was discontinued because of suspected toxity, and the temperature again rose in spite of improvement in the cerebrospinal fluid Soon afterwards, however, there was clear evidence of recrudescence, with a second spike of temperature. During these two episodes of fever, no organisms were grown from the cerebrospinal fluid, but later *E. coli* was isolated from a loculus. The temperature chart of [illegible]

[illegible]

aureomycin inhibited the organism (on one occasion for 3 weeks), but immediately it was stopped the organism again multiplied: that finally intrathecal polymyxin appeared to cure the disease, but that this may have been coincidental, for the decreasing spikes of temperature were evidence that the disease was burning itself out. This patient was very ill on many occasions, but eventually recovered completely.

Features peculiar to post-operative meningitis

Loculi.—The presence of a brain wound renders treatment more difficult at every stage, for not only does a ragged cavity containing brain debris provide an excellent culture medium, it is a backwater unlikely to be freely irrigated by drug-containing cerebrospinal fluid, and organisms, some of which are capable of gross brain destruction, may be enclosed within its avascular depths. Moreover, blood and debris will find their way into the cerebrospinal fluid and will facilitate blocking of subarachnoid pathways. These conditions are ideal for the formation of an infected loculus. An escape of cerebrospinal fluid and debris through the dural opening, moreover, not infrequently results in an extracranial loculus; particularly important in occipital craniotomies, where pockets are readily formed in the depths of the cervical muscles. Intermittent leakage of such fluid collections into the cerebrospinal fluid will produce meningeal reactions. Some will be sterile, due to irritant breakdown products in the

loculated fluid (Finlayson and Penfield, 1941), but our experience is that most are bacterial and the organism will be discovered by careful examination of the loculus fluid, even when repeated cultures of the cerebrospinal fluid are negative.

Cerebrospinal-fluid fistulae and hydrocephalus.—Meningitis following operation may also be complicated by (1) a leak of cerebrospinal fluid from the wound; (2) alteration in the flow of cerebrospinal fluid as a result of a short-circuit operation; or (3) a pre-existing hydrocephalus influencing the volume and circulation of the cerebrospinal fluid. It is our experience that meningitis associated with a leak can rarely be controlled until the wound has closed, and where ventriculostomies have been made it is often impossible to attain a therapeutic level of sulphonamide or systemically administered antibiotic in the spinal subarachnoid space. This is evidence that the larger amount of the drug enters the cerebrospinal fluid by way of the choroid plexus, and is short-circuited with the fluid through the ventricular opening. Finally, it is not surprising that infections are more difficult to control in the presence of a large hydrocephalus.

Treatment

In addition to the routine treatment of the meningitis, the following surgical measures may be necessary, and it must be remembered that in hydrocephalus the effective intrathecal dosage of antibiotic will vary with the volume of cerebrospinal fluid.

(1) Severe cerebrospinal-fluid leaks must be closed by wound re-suture if the patient's condition permits this to be done; reduction of the cerebrospinal-fluid pressure by frequent lumbar punctures or a short period of continuous drainage of the ventricle, or the spinal theca, may be helpful, but a hypodermic needle placed through the skin flap of a leaking wound so that it lies in the subjacent lake of cerebrospinal fluid and connected by tubing to a bottle has proved to be the safest and surest method of aiding healing

(2) Infected loculi should be needled and antibiotics instilled: on occasion evacuation of a large cavity full of infected debris and careful remaking of the wound will produce striking improvement.

Prophylaxis

As regards prophylaxis, all steps must be taken to ensure wound healing and the prevention of cerebrospinal-fluid leaks and loculi by the observation of correct technique. Lumbar puncture and wound aspiration should be done when necessary, dural defects over large cavities closed by a fascial graft (this has the advantage over synthetic membranes in that it rapidly adheres and forms a watertight closure) and potential dead space in muscle layers obliterated by careful suture. Where air sinuses are widely opened inadvertently it is advisable to close them by a strip of fascia sutured in position; there is little risk from immediate meningitis, but unless closed, infected air may be blown into the wound causing infection with loss of the bone flap and perhaps subsequent meningitis. Where basal meningiomas and neuromas have widely invaded the petrous bone, the dura should be repaired by fascial graft to obviate the risk of infection spreading from the ear.

Infection has a higher incidence after long operations and in wounds that are re-opened maybe months later, and is notorious after large tumour removals from the posterior fossa. Sulphonamides may be given prophylactically, and penicillin and Sulphamezathine powder are usually insufflated into the wound at the end of the operation.

TUBERCULOUS MENINGITIS

The value of streptomycin in the treatment of this dread disease has now been established beyond doubt. At first, toxic reactions to the drug, sometimes catastrophic, the distaste of physician and patient alike for prolonged daily lumbar punctures, uncertainty as to how long treatment should be continued and what the end-result was going to be, but certainty of relapse if treatment were reduced at the first welcome sign of recovery, combined to create an atmosphere of gloom and discouragement. However, in several centres treatment was meticulously pursued, and reported recoveries increased in number; nor were they all invalids, some were well and active and did not relapse. Much credit for this progress belongs to the late Sir Hugh Cairns and his team at Oxford, where segregation of cases, careful specialized nursing and exact observation of the cases at all stages combined to provide the improved results.

Subarachnoid exudates

Not unnaturally search was made *post mortem* for the cause of failures: accumulations of organized exudate were noted, sometimes involving blood vessels and

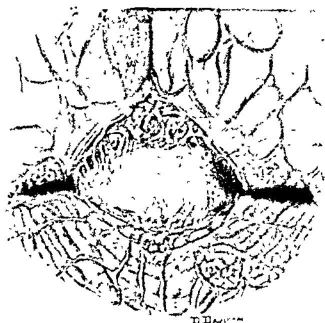


FIG. 75.—Tuberculous meningitis. Drawing of posterior aspect of mid-brain; the occipital lobes have been elevated from the upper surface of the cerebellum to show the dense organized adhesions closing off the subarachnoid space of the cisterna ambiens, and binding the cerebral hemispheres and cerebellum to the mid-brain. (Sir Geoffrey Jefferson's case.)

causing thrombosis with infarction and "atrophic" hydrocephalus, but sometimes causing hydrocephalus by blocking subarachnoid pathways, especially in the basal cisterns and around the incisura of the tentorium (Fig. 75); more rarely the iter and foramina of the fourth ventricle were obstructed. These observations, together with the fact that cisternal and lumbar puncture not infrequently demonstrated subarachnoid block just prior to death, and the knowledge that streptomycin did not rid the subarachnoid pathways of the *Mycobacterium tuberculosis* very rapidly, naturally led to the supposition that exudative reaction prevented access of the streptomycin to entangled tubercle bacilli, and so various methods were evolved in the hope of combating this difficulty.

These methods were: (1) The use of streptokinase to soften the exudate and facilitate penetration by streptomycin (Cathie and MacFarlane, 1950). (2) Surgical procedures in which tubes for the instillation of streptomycin were placed at the "black spots" of exudative block, for instance the chiasmatic and ambient cisterns. These were used variously either when blocks appeared or initially in order to prevent

their development; but where a block was present it seemed unlikely that the streptomycin would reach the organism with any greater readiness, and in the absence of a block a tube would appear to be unnecessary (Cairns, 1951). (3) The use of P.P.D. tuberculin in desperately ill cases was shown to be effective in a certain number of cases (Smith and Vollum, 1950). This feature in the pathology, however, is not peculiar to tuberculous meningitis; it is present in any chronic meningitis, and is not likely to occur if treatment is early and effective. Thus, although the methods mentioned above, especially the last, have played some part in improving results, the most striking change has been the improvement using streptomycin alone, the dose of which should be 100 milligrams intrathecally daily for 6 weeks, and 1 gramme intramuscularly daily for 3 months, with no rest periods. Earlier diagnosis, confidence in the method, so that treatment is maintained whatever the patient's condition, streptomycin of improved quality, and adjuvants such as para-aminosalicylic acid and izoniazid have resulted in a recovery rate nearer 80 per cent than the first proud attainment of 50 per cent. Late relapses, however, claim more victims (Russell, Sheenah and MacArther, 1953). It is certain that intramuscular streptomycin alone is far less effective than combined therapy (Levinson and his colleagues, 1950).

Surgical treatment

As in the case of non-tuberculous meningitis, more effective antibacterial treatment has lessened the need for surgery. But if progress is not smooth, surgery may be required.

Burr holes

These may be necessary in order to inspect the subdural space (one case of subdural effusion has been seen (Turner, 1953), or to tap the ventricle and instil streptomycin.

Another use for burr holes is during the making of ventricular studies in order to demonstrate the cause of raised intracranial pressure.

Operations for the relief of hydrocephalus

Temporary drainage may be necessary during the active phase, but if so the disease will be so severe and extensive that recovery is unlikely; progressive hydrocephalus following cure is rare and should be treated as shown in the section dealing with complications.

Treatment of tuberculous abscesses and tuberculomas

These rarely complicate, but may be a hidden cause of tuberculous meningitis; in either case tuberculous abscess should be considered where deterioration is unexplained (Cairns, 1951) Focal signs, even if transient, or persistently raised intracranial pressure should be investigated. In this the electroencephalogram and especially ventricular studies, using Myodil when the pressure is high, are most valuable.

Recently a young woman was transferred from a fever hospital where she had been admitted 5 months previously, severely ill with miliary tuberculosis and tuberculous meningitis. Improvement was rapid on the usual treatment, but although the cerebrospinal-fluid cells fell, the protein rose and she complained of headache and vomiting. Finally, although bright and lucid, she began to have hydrocephalic attacks of alarming severity and papilloedema was observed. A Myodil ventriculogram (Fig. 76*a*) demonstrated a right cerebellar space-occupying lesion, and operation disclosed a tuberculous abscess (Fig. 76*b*) which was dissected out under a screen of streptomycin; recovery was uncomplicated.

It is clear that streptomycin is most effective against the *Myobacterium tuberculosis*; the safety with which tuberculomas can be excised and extradural spinal abscesses or

SURGERY OF THE PRIMARY LESION

Attainment of a high degree of mastery over acute meningitis has brought into prominence a new aspect of surgery; that is the search for and treatment of the primary focus as a safeguard against further episodes of infection; rarely now should a primary focus be a chance finding demonstrated at necropsy.

Infection by such organisms as staphylococci, streptococci and *Escherichia coli* (except in infants) is rare in uncomplicated primary meningitis and suggests spread from a neighbouring focus. However, search should be made in all cases, whatever the organism, for a possible portal of entry, be it a breach in the dura, a dermal sinus approaching the meninges, or extradural, subdural or intracerebral suppuration.

Some of the primary lesions are only too obvious; others are obscure, and their betrayal by a wave of meningitis provokes an interesting and absorbing search. Not all foci will be discovered, for example local cortical infection may remain hidden whilst the patient is ill, and will be evident later only as a cause of persistent neurological defect. Moreover, there still remain many problems in treatment. The diagnosis and treatment of the less obvious lesions are considered in the following paragraphs.

Trauma

Meningeal infection resulting from open wounds of the head and spine, as common in war as they are rare in peace, differs in no way from post-operative meningitis which has been considered on page 149.

Closed head injuries by virtue of causing breaches of the dura mater overlying fractured paranasal air sinuses or tegmen tympani in an unknown number of cases constitute a problem of great magnitude. Early deaths from meningitis do occur and in the absence of careful autopsies on all fatal head injuries are probably more common than is realized. Yet diagnosis is difficult, requiring elaborate investigation, and definitive treatment is often extensive. Not infrequently death from unsuspected meningitis is reported at inquests on head injuries, and in Fig. 77 are the tracings of fractures of 3 patients who died from early meningitis in a hospital during the same year; all were initially unconscious for very brief periods and showed on admission every prospect of an early and complete recovery; all had fissured fractures of the frontal bone approaching the skull base, but none was severe and there was no displacement, and rhinorrhoea was neither complained of nor observed. Success or failure in the treatment of such cases depends on adequate prophylaxis with sulphonamide and maximal antibiotic therapy where meningitis has supervened; repair of the defect may be necessary if a persistent cerebrospinal-fluid leak is preventing control of meningitis, but ideally operation should be postponed until later. Such cases serve to demonstrate the desirability of early x-ray examination of the skull in all head injuries, for although fractures are unimportant in the majority of cases, fractures approaching the base should warn of the risk of meningitis (Calvert, 1942) and knowledge of the site and nature of the fracture may be most useful when searching for an extradural haemorrhage. The diagnosis of meningitis is not easy in the recovery phase of a head injury when the patient is ill, and may be stuporose, and where subarachnoid blood may give rise to all the signs of meningitis. Furthermore, treatment is less likely to be successful when infection is accompanied by severe brain damage. The mechanism of fracture in which small pieces of paranasal sinus roof are uplifted and damage the overlying brain, which frequently fills and plugs the underlying air cell, has been described elsewhere (Johnson and Dutt, 1947). This sequel of the injury provides the means by which air may gain access to brain tissue and produce aeroceles and traumatic ventriculograms; it accounts for delayed rhinorrhoea as the softened cerebral plug is disturbed in the sinus by changes of air pressure, and

is the reason ...
weeks, but fo
plications by ... the dural defect by a patch of fascia (Cushing, 1927). The difficulty however is to be sure of the presence and of the site of such a defect. Gross comminution will leave no doubt as to the existence of a dural-sinus communication, but defects can occur in the absence of fissuring or displacement; danger zones are the middle ethmoidal roofs and the sphenoidal bulge of the anterior pituitary wall (Fig. 72, page 150). Radiographic examination of this region is difficult, but oblique stereoscopic projections of the orbits may reveal defects (Johnson and Dutt, 1947). Anterior

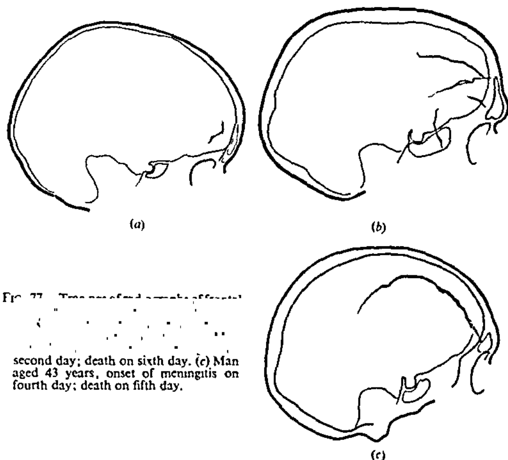
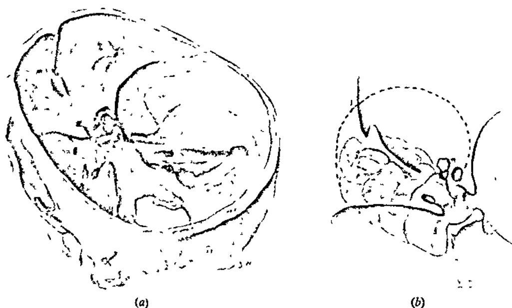


Fig. 77 ... second day; death on sixth day. (*c*) Man aged 43 years, onset of meningitis on fourth day; death on fifth day.

fractures are easy to diagnose, middle ethmoid less easy, and sphenoidal most difficult of all, but the structure of the anterior sella wall may be visualized radiologically and damage recognized (Fig. 78). As treatment improves, the diminishing danger of waves of meningitis must be weighed against the risk and disadvantage of definitive operation, and perhaps a negative exploration. Experience suggests that the following indications for exploration should be adopted: (1) severe, prolonged or delayed rhinorrhoea or otorrhoea (prolonged and profuse rhinorrhoea, perhaps lasting for years, almost certainly means a leak from the basal cisterns by way of the sphenoidal sinus); (2) meningitis; (3) aerocele, (4) abscess; (5) radiological evidence of a sinus-roof defect.

In fact there should be evidence either of a large comminution (anosmia will lend support to this) or that infection has crossed the dura. Cases of transient rhinorrhoea or anterior fossa fracture have not been explored unless there has been clear radiological evidence of a defect; in this connexion it is of interest that in association with short-lived rhinorrhoea, x-ray examination may show a small amount of air in the

subarachnoid space and yet no dural defect be demonstrable at subsequent operation: the portal of entry almost certainly is by way of the olfactory filaments temporarily loosened in their canals by the injury. Aerocele, however, is unequivocal evidence of a large defect with some cortical laceration; its time of appearance and rate of increase in size will depend, in part, on the extent of the initial brain damage. Radiological examination of the skull is worth repeating in the first few weeks after injury, especially if facial bones have been manipulated, for aeroceles occasionally appear after this when in all other respects recovery from the injury appears to be *complete.*



(*a*) (*b*)

Surgical treatment

Otorrhoea, the result of a fissure in the tegmen tympani and a linear dural tear, usually ceases and healing is safe. The occurrence of meningitis or delayed profuse otorrhoea, however, is an indication for dural repair by a subtemporal approach.

severe disabilities. It is not surprising therefore that the best results are not attained *unless the defect is first exactly localized by careful radiography and then a limited* planned operation carried out under good anaesthesia when the patient has recovered from the acute head injury.

The operative *approaches should be varied according to the fracture site,* so that there is minimal retraction of frontal lobes and damage to intact olfactory tracts is avoided. An extradural repair of frontal or anterior ethmoidal defects caused by the not uncommon transverse fracture at the base of the crista galli *is illustrated in Fig. 79a.* Intradural inspection on both sides excludes defects farther back; fascia may then be placed across the mid-line extradurally without damaging the olfactory bulbs. The

usual method of exposure for the common fracture of the middle ethmoid roof shown in Fig. 79*b*; fascia lata or temporal fascia is laid over the defects intradurall it need not be sutured down. The repair of a sphenoidal defect is shown in Fig. 79 a defect diagnosed radiologically (*see* Fig. 78). A large low right-sided flap is turnec extending sufficiently over the mid-line to enable an intradural inspection to be mad

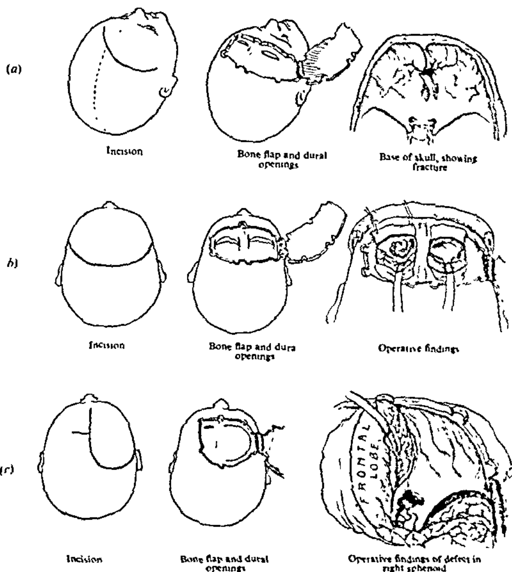


FIG. 79 —Operations for repair of dural sinus defects (*a*) Extradural repair of fracture of crista galli Intradural inspection has excluded a second defect. (*b*) Intradural repair of fractures of both middle ethmoids. (*c*) Intradural repair of right sphenoidal defect, anterior intradural inspection on the left.

to exclude a left anterior defect. The right side is then approached along the sphenoidal wing and the olfactory tracts are elevated with the brain (and preserved) and any defects posterior to the crista galli on either side are readily brought into view.

There still remain a group of cases in which exploration is negative, and provided leakage is not through the middle ear and eustachian tube, it must be by way of the sphenoidal sinus, perhaps from the sella region or from a middle fossa extension (Fig. 72). Packing the sphenoidal sinuses with muscle from above is an effective method of stopping the leak (*see* page 164).

Congenital dermal sinuses

Attention has been drawn recently to the importance of the search for congenital dermal sinuses in otherwise unexplained meningitis by Matson and Ingraham (1951), by Logue and Till (1952), and by Cardell and Laurence (1951).

They first report cranial sinuses in 10 children, 8 of whom had dimples and palpable masses, 7 occipital and 1 bridge of nose. In 4 of these there was inflammation round the sinus openings which drained thin fluid. Meningitis was the primary consideration in 5 patients (50 per cent) and the organisms were all staphylococci resistant to penicillin. They point out the likelihood of intracranial extension and the poor results of surgery if meningitis has already occurred. This is confirmed by Logue and Till who analysed 32 cases of posterior fossa dermoid cysts and found that 10 of these had dermal sinuses; they point out that 3 of their own 4 cases in this category had intracranial infection, the organisms being *Staphylococcus aureus*, *E. coli* and *B. proteus*. Postero-anterior or half-axial radiographs of the skull are diagnostic, showing a mid-line occipital bone defect with sclerosed margins. This is the excavation of the inner surface of the occipital bone produced by the intracranial dermoid (Fig. 80*a*). Sometimes the channel through the bone carrying the dermal sinus may be seen as a furrow or minute hole above the defect (Fig. 80*b*).

Cardell and Laurence, reporting on 34 cases of dermal sinus (including 2 cranial) collected from the literature, and one fatal spinal case of their own, emphasize the importance of carefully examining suspected "pilonidal" sinuses of the lumba-sacral region, especially if the opening is situated some distance from the anus. Dermal sinuses may communicate with, or end in close proximity to, the spinal meninges and associated meningitis is not uncommon, if the organism is of low virulence, the slow upward spread of infection and rigidity may straighten the spinal curves so gradually that the clinical sign of "unfolding of the spine" is produced. These authors point out that radiographs may show evidence of spina bifida (16 out of 34 cases), and make the most interesting observation in their own case that it may be embryologically a *forme fruste* of diastematomyelia. Fully developed diastematomyelia has been described in association with a dermal sinus and the following case illustrates this pathology.

CASE IV.—D.McG., aged 2 years. "Pilonidal" sinus excised, recurrent meningitis;

whole of the stained area was excised. Healing was normal. Histology showed a central subcutaneous track lined by cornified squamous epithelium; there was no hair. Two months later he became drowsy and vomited, and was admitted to hospital where meningitis due to *E. coli* was discovered, and treatment with streptomycin resulted 3 weeks later in apparent cure. However, he had three more attacks during the next 6 months, and all responded to streptomycin or chloramphenicol. On several occasions the fluid was blood stained and in each attack organisms were seen in the smear. Because of the possible connexion with the pilonidal sinus he was referred for neurological treatment. The scar was excised and deepened to one side of the lumbar spine. It was then noticed that a cord ran

Cerebrospinal-fluid fistulae

Apart from trauma, cerebrospinal-fluid fistulae may develop spontaneously where erosion of dura, especially subjacent to basal cisterns, occurs as a result of expansion

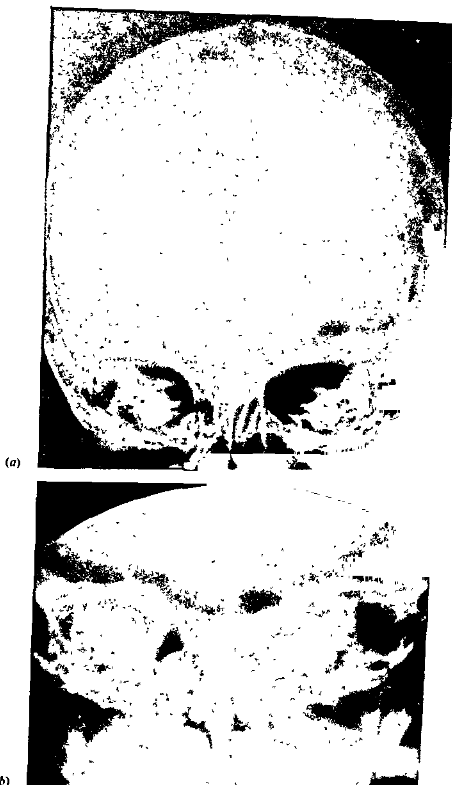


FIG. 80.—Radiographs of occipital dermal sinuses. (a) Shows the sclerosed [illegible] and above it [illegible] a child [illegible] until [illegible] brought [illegible]

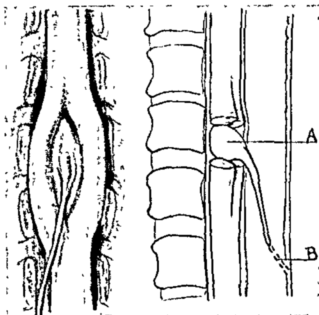


FIG. 81.—Diastematomyelia and dermal sinus. The dermal sinus approaches the dura and expands into a sac which lies between the bifid theca (diastematomyelia). *B* was excised as a pilonidal sinus; *A* was removed subsequently because of recurring meningitis.



FIG 82—Pituitary adenoma Encephalogram showing the suprasellar extension of a pituitary adenoma arising above a very much enlarged sella. Sudden death from meningitis occurred at home whilst awaiting admission for operation

of tumours or cysts in relationship to paranasal sinuses. The leak may be sufficient to cause the patient to complain, but frequently it is only as a result of close questioning on recovery from an attack of meningitis that a watery nasal, *naso-pharyngeal* or aural discharge is recollected. Skull x-ray examination, which should be routine in unexplained meningitis, may reveal a totally unexpected lesion.

Rhinorrhoea

Rhinorrhoea may be produced by osteomas and mucoceles of the ethmoids (Cushing, 1927) or by mucoceles of the sphenoid eroding the anterior sella wall in



FIG. 83.—Arachnoidal cyst. Air encephalogram showing air-containing cyst (arrowed in the inset), eroding the sella turcica; this is marked by a dotted line. A Myodil ventriculogram showed a normal third ventricle (tracing superimposed on the encephalogram).

front of and above the pituitary gland. Adenomas of the pituitary occasionally cause meningitis by erosion through the diaphragma sellae above and into the sphenoidal sinus below (Fig. 82), and it is remarkable that so few pituitary tumours are complicated in this way. Other tumours in this region may also cause destruction and open cisterna chiasmatis into the sphenoidal sinus, and rarely arachnoidal cysts enlarge the sella and rupture into the sphenoid. Fig. 83 shows the air encephalogram of a case in which profound meningitis followed a few weeks of rhinorrhoea; the only other symptom was primary amenorrhoea. Air studies demonstrated a large arachnoidal cyst eroding the sella, and a Myodil ventriculogram showed that the third ventricle was neither involved in the fistula nor indented by a subjacent tumour or cyst.

Treatment.—Closure of a defect by fascial grafting presents no problem in the ethmoidal roof region, but leakage *via* the pituitary fossa is extremely difficult to treat. In the case of arachnoidal cysts and unencapsulated adenomas it may be necessary to open widely into the sphenoidal sinus from above, remove the anterior wall of the sella and pack muscle between the pituitary capsule and the muco-

periosteum which is stripped forwards, so that muscle fills the bony cavity of the sphenoidal sinus or sinuses Leakage by way of a pituitary adenoma (Fig. 82) may cease after operation if there is a capsule which can be packed with muscle, or it may cease spontaneously.

Otorrhoea

Otorrhoea may be associated with cholesteatomas of the petrous, primary or secondary to a chronic mastoid infection.

Treatment.—This consists in removal, followed by a fascial graft. The following case illustrates this.

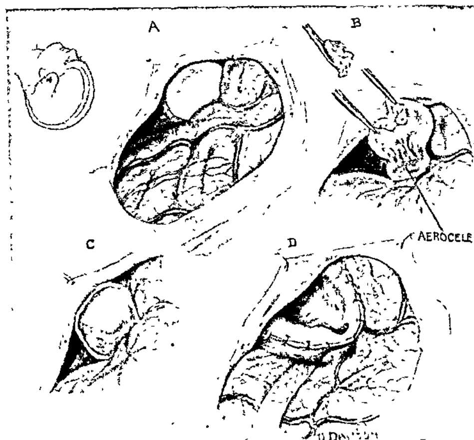


Fig. 84.—Otitic cholesteatoma and aerocele, operative findings. In *A* the cholesteatoma is exposed under the left temporal lobe. In *B* the aerocele is seen burrowing into the left temporal lobe. *C* is the cavity in the petrous bone after removal And *D* illustrates the patch of fascia sutured across the defect.

CASE V.—W B, aged 47 years. Mastoiditis followed by meningitis, cerebrospinal-fluid otorrhoea and meningitis, cholesteatoma; acute dysphasia caused by aerocele.

This patient underwent a simple mastoidectomy at the age of 21 years; following this he was extremely ill and probably had meningitis, but he eventually recovered and was well, apart from "blackouts" occurring about once a year, until 15 years later, when there was a recurrence of mastoiditis and meningitis, and a further operation was done. The ear discharged occasionally, but 17 years after the onset there was a sudden outpouring of clear fluid from the ear which lasted a few days and soaked several handkerchiefs. A mild attack of meningitis followed this. He continued well, apart from "blackouts", until 3 weeks before his admission (24 years after the onset), when he suddenly became severely dysphasic Radiographs showed air in the right temporal lobe and exploration exposed the

sac of an aerocele lying above a cholesteatoma which was rising out of a chronic ear cavity. Cholesteatoma accessible from above was removed and a patch of fascia sutured over the defect (Fig. 84). Two years after this there was further discharge from the ear and the wound was reopened; cholesteatoma had reformed in the petrous cavity, but the fascial graft was intact and there was no intracranial extension. The cholesteatoma was removed extradurally from above and later through a mastoid approach, and he has had no further trouble.

Extradural infection

This is by far the most important cause of secondary meningitis; it follows infection commonly in the cavities of the ear, and also in the paranasal sinuses, or osteomyelitis of bone where it adjoins dura mater.

Aural infection

Acute otitis.—Acute otitis may be complicated by meningitis, and if so it usually follows sinus thrombosis with a typical clinical picture, which is less striking, of course, if suppressed by antibiotics, and may be associated with local damage as evidenced by focal neurological signs, the result of cortical thrombophlebitis or localized meningitis. The organism will commonly be a staphylococcus, streptococcus, or pneumococcus, sensitive to penicillin; and as it is unusual for meningitis to develop in the first few hours of the disease, effective treatment, antibiotic and operative, as indicated will avert this complication in most instances.

Chronic otitis.—Meningitis may occur without warning in a patient who has a chronic discharging ear; it may be insidious in its onset (*see* page 137) and the organisms of low virulence, probably at most times saprophytic in the ears (*B. proteus*, *E. coli*, *Ps. aeruginosa*), and difficult to eradicate because of resistance to antibiotics

In most instances an attack of meningitis indicates that the ear disease has recently advanced and that further complications have occurred, for example petrositis, extradural abscess, or brain abscess, which have not been unheralded; Jefferson (1950) has emphasized the importance of pain in this connexion. Pain in a chronically discharging ear, at least, means a spread of infection in the bone, and usually means that the dura is involved with the strong possibility that infection has passed through It is an indication for urgent treatment of the ear, and for the search for brain abscess.

Paranasal sinuses

Transient sinusitis may result in meningitis or brain abscess, and often so fleeting has been the sinus infection that there is no evidence of it when the patient comes under treatment. Suppurative sinusitis, severe or of long standing, may cause osteomyelitis of the thin sinus roof, extradural abscess, subdural abscess, or brain abscess; meningitis may be a complication at any stage. At the outset the patient may be acutely ill and in severe pain, so that there can be little difficulty in making the diagnosis; or the sinus infection may be quite silent, the posterior frontal wall, for example, disappearing without a symptom. Spreading osteomyelitis of the frontal bone or of the skull base and cavernous sinus thrombosis were dreaded complications of sinusitis before antibiotics were available. Now they are rare, but subdural empyema, brain abscess and spread of infection to the pituitary fossa itself from the sphenoid, heralded, accompanied or complicated by meningitis, may occur before there has been any indication for antibiotic therapy.

Treatment is that of the local disease, and must be special to each case, as the following illustrates.

CASE VI.—M. H., aged 14 years. Suppurating ethmoidal sinusitis; meningitis; ethmoidal drainage; subdural empyema; drainage of empyema and graft to dural defect over middle ethmoid.

A girl of 14 years had been well until 1 week before admission, when she complained of severe pain in the right eye, shortly followed by headache and gross swelling of the eyelid. She was admitted to the local hospital and treated with penicillin. On the day before admission, a right external ethmoidectomy had been done, and pus in contact with dura of the anterior fossa evacuated. Lumbar puncture on the operating table produced a turbid fluid with 550 leucocytes; she clearly had meningitis, and 16,000 units of penicillin were injected intrathecally The next day she was drowsy, and commenced to have convulsive attacks confined to the left face and arm; it was because of this complication that [illegible]

tous brain immediately plugged the burr hole and prevented further drainage, and in view of the strong possibility that the infection was still spreading from ethmoidal cells, a frontal craniotomy was made. Pus was evacuated from all aspects of the swollen frontal lobe, which was coated in a sheet of fibrinous pus which had to be peeled off. The frontal lobe was retracted and pus could be seen welling up from a defect in the dura over the right middle ethmoid The entire field was washed with saline solution and a patch of temporal fascia was laid across the defect. Tubes were left in position for the subsequent instillation of penicillin. Recovery was rapid and complete, save for epileptic attacks, of which there have been some 3 or 4 a year since

Of special interest and importance are the infected mucoceles of the sphenoidal sinus which may simulate pituitary tumours, and which may involve the pituitary gland in the infective process, giving rise to pituitary cachexia associated with recurrent meningitis.

Treatment if at all feasible must be on the lines indicated under rhinorrhoea, page 164.

Osteomyelitis of the skull

This is usually secondary to osteomyelitis elsewhere, or sinusitis, and is now less common. However, the importance of full-thickness excision of diseased bone in order to prevent relapse and avert intracranial infection has not diminished. It should be recorded that staphylococcal infection treated by penicillin may very closely resemble tuberculous infection.

Osteomyelitis of the occipital bone requires mention because of the difficulties of diagnosis: this may be secondary to osteomyelitis elsewhere, but usually follows a skin infection and if untreated is very liable to result in meningitis and, curiously, often presents as multiple cranial nerve palsies due to localized meningitis in nerve-root pockets. Difficulty arises because the signs of inflammation may be completely absent and the patient may complain only of occipital pain. Sufficient time may not have elapsed for bone changes to be visible on x-ray examination, and operation may have to be undertaken solely on account of severe localized pain, especially if accompanied by pyrexia and leucocytosis, or by the slightest sign of intracranial involvement.

Osteomyelitis of the spine

Acute diffuse extradural spinal abscess has been illustrated (Case I), but non-tuberculous infection involving bone and disc may present as a localized collection of pus anterior to the dura, and may cause cord compression; if untreated, meningitis will result. Such an abscess arising from an infected pharyngeal pouch has caused osteomyelitis and acute softening of the disc between C.6 and C.7, with cord compression. At operation there was no pus posterior to the dura, but the spinal cord was com-

pressed by an anterior extradural abscess containing softened sequestrated disc tissue. Although there was no general meningitis, there was a localized collection of pus, which grew anaerobic streptococci on culture, round the left seventh cervical nerve roots (Fig. 85). This finding is of interest in demonstrating the mode of spread of infection, which may occur without any evidence of meningitis. Perhaps more remarkable in this connexion were the findings in another patient who developed a granuloma in the cervical cord following osteomyelitis of the cervical vertebrae. At operation there was a granulomatous track running down inside the dura from a nerve-root sleeve to the spinal cord. Culture of this track and of the diseased area of the cord grew *Staphylococcus aureus*, although there had never been clinical meningitis, and the vertebral disease had been quiescent for years.

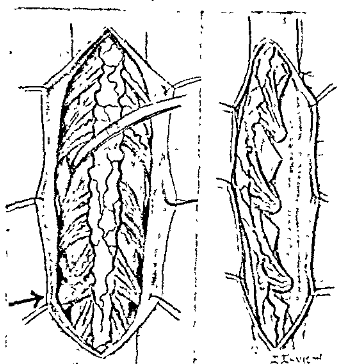


Fig. 85—Anterior extradural abscess. Tense swollen cervical cord exposed by laminectomy; round the left seventh roots are a few beads of pus (arrowed). The lateral view shows how the anterior extradural abscess flattens the cord to give the appearance of an intramedullary tumour.

Subdural empyema

Although regarded as synonymous with loculation abscess (Alexander, 1949), it has an importance of its own as a primary condition, not necessarily, although usually, accompanied b[illegible] of brain abscess, or more commonly of extradural [illegible]litis, sinusitis or otitis. It may be localized, but [illegible] has a tendency to spread along the falx and to loculate posteriorly where it is most dependent as the patient lies in bed: this was not unknown to Monro, who in 1827 described the day-to-day progress of a case in which at necropsy pus was found to have tracked beneath the tentorium.

The subarachnoid space closes off early and on rare occasions the cerebrospinal fluid may be normal. Underlying cortex is involved by oedema and thrombophlebitis, and sometimes becomes densely scarred, a potent source of subsequent epileptic seizures. Typically the patient will be ill and pyrexial on admission and within a short space of time repeated focal convulsions will be followed by dense paralysis spreading down one side of the body.

If the source of infection is the ear, hemianopia will be produced as the pus spreads under the occipital lobe, to be followed by weakness of the leg as it travels forwards along the falx, and finally the arm will be involved as the pus overflows on to the

convexity of the hemisphere anteriorly. Burr holes made in the parietal, temporal or occipital regions in search of a brain abscess or subdural pus, will expose normal cortex, and needling will be negative unless (and this is very important) the cannula is directed on to the falx, when aspiration will produce a varying amount of pus.

When draining an extradural abscess, a problem arises as to whether the dura should be opened in the search for subdural pus. Although the risk of meningitis, if a normal subarachnoid space is exposed, is very much less with chemotherapy, it is advisable to explore the subdural space through a discrete burr hole at a distance, if there is any doubt.

Treatment is early drainage by multiple burr holes and the emplacement of tubes for the instillation of antibiotics. In certain cases it may be necessary to turn a flap (*see* Case VI). It is important to place additional burr holes posteriorly and medially to obtain dependent drainage, and where progress is arrested there may be a need to explore the subdural space over the cerebellar hemispheres. The causal organism is commonly the streptococcus, sensitive to penicillin (Schiller, Cairns and Russell, 1948).

Brain abscess

It is probably not widely realized that many cases of brain abscess present as meningitis (25 per cent in the Manchester Unit), and that it is only when the meningitis has been treated that the abscess begins to show some evidence of its presence

Meningitis and brain abscess may be associated in three ways: (1) meningitis may occur as infection crosses the subarachnoid space from nasal sinus or ear to the brain, and an abscess form whilst the meningitis is under treatment; (2) meningitis may be the result of leakage or rupture of a brain abscess; (3) meningitis may result in brain abscess (*see* page 155)

Early and adequate treatment of the meningitis and primary focus will reduce the likelihood of brain abscess developing simultaneously or subsequently. It is most important, however, to recognize the cases of meningitis which have a brain abscess as a primary focus. Sometimes, as for example in chronic aural infection, abscess is to be expected, but more usually persistent or increasing neurological defects following partial or complete recovery from the acute attack of meningitis or unexplained relapses will point to the diagnosis. Papilloedema, rising pressure of a cerebrospinal fluid which contains a few cells and an increasing amount of protein will be more suggestive. However, slight clinical disimprovement not reflected by gross changes in the cerebrospinal fluid, but, most significant of all, apathy and drowsiness, are urgent indications to search for abscess.

In this, the electroencephalogram has great value, for it is unlikely that a cerebral abscess will be present in the absence of slow delta activity focusing at or around the abscess site, and where such a focus exists a burr hole should be cut and a search made by cannula if there is the remotest possibility of suppuration within the brain. Treatment consists in frequent aspiration and the instillation of penicillin in high concentration (500,000 units in 1 millilitre), or other antibiotic if indicated by sensitivity tests. Progress is watched by means of Thorotrast pyograms. In certain circumstances the abscess should be excised, especially if aspiration is not proving satisfactory. Cerebellar abscesses usually give rise to unequivocal focal signs, but do not always do so, and in this group the observation that all is not well (apathy, drowsiness, unexplained earache or headache), fortified perhaps by the knowledge that at the time the mastoid was cleared there was diseased bone or extradural pus adjacent to the posterior fossa, will be the evidence on which the [illegible]
the posterior fossa [illegible]
missed, and in the c [illegible]
frequent aspirations that immediate excision of the abscess capsule provides the best results in most cases (Pennybacker, 1950; Botterell and Drake, 1952).

pressed by an anterior extradural abscess *containing* softened sequestrated disc tissue. Although there was no general meningitis, there was a localized collection of pus, which grew anaerobic *streptococci* on culture, round the left seventh cervical nerve roots (Fig. 85). This finding is of interest in demonstrating the mode of spread of infection, which may occur without any evidence of meningitis. Perhaps more remarkable in this connexion were the findings in another patient who developed a granuloma in the cervical cord following osteomyelitis of the cervical vertebrae. At operation there was a granulomatous track running down inside the dura from a nerve-root sleeve to the spinal cord. Culture of this track and of the diseased area of the cord grew *Staphylococcus aureus*, although there had never been clinical meningitis, and the vertebral disease had been quiescent for years.

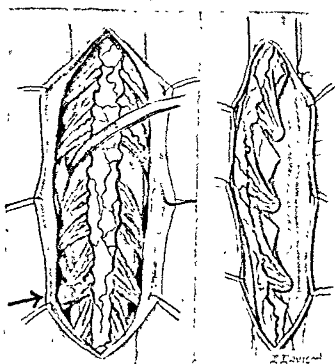


FIG. 85—Anterior extradural abscess. Tense swollen cervical cord exposed by laminectomy; round the left seventh roots are a few beads of pus (arrowed). The lateral view shows how the anterior extradural abscess flattens the cord to give the appearance of an intramedullary tumour.

Subdural empyema

Although regarded as synonymous with loculation abscess (Alexander, 1949), it has an importance of its own as a primary condition, not necessarily, although usually, accompanied by meningitis. It is a complication of brain abscess, or more commonly of extradural infection associated with osteomyelitis, sinusitis or otitis. It may be localized, but characteristically is extensive, and has a tendency to spread along the falx and to loculate posteriorly where it is most dependent as the patient lies in bed: this was not unknown to Monro, who in 1827 described the day-to-day progress of a case in which at necropsy pus was found to have tracked beneath the tentorium.

The subarachnoid space closes off early and on rare occasions the cerebrospinal fluid may be normal. Underlying cortex is involved by oedema and thrombophlebitis, and sometimes becomes densely scarred, a potent source of subsequent epileptic seizures. Typically the patient will be ill and pyrexial on admission and within a short space of time repeated focal convulsions will be followed by dense paralysis [illegible] one side of the body.

[illegible]

along the falx, and finally the arm will be involved as [illegible]

convexity of the hemisphere anteriorly. Burr holes made in the parietal, temporal or occipital regions in search of a brain abscess or subdural pus, will expose normal cortex, and needling will be negative unless (and this is very important) the cannula is directed on to the falx, when aspiration will produce a varying amount of pus.

When draining an extradural abscess, a problem arises as to whether the dura should be opened in the search for subdural pus. Although the risk of meningitis, if a normal subarachnoid space is exposed, is very much less with chemotherapy, it is advisable to explore the subdural space through a discrete burr hole at a distance, if there is any doubt.

Treatment is early drainage by multiple burr holes and the emplacement of tubes for the instillation of antibiotics. In certain cases it may be necessary to turn a flap (*see* Case VI). It is important to place additional burr holes posteriorly and medially to obtain dependent drainage, and where progress is arrested there may be a need to explore the subdural space over the cerebellar hemispheres. The causal organism is commonly the streptococcus, sensitive to penicillin (Schiller, Cairns and Russell, 1948).

Brain abscess

It is probably not widely realized that many cases of brain abscess present as meningitis (25 per cent in the Manchester Unit), and that it is only when the meningitis has been treated that the abscess begins to show some evidence of its presence.

Meningitis and brain abscess may be associated in three ways: (1) meningitis may occur as infection crosses the subarachnoid space from nasal sinus or ear to the brain, and an abscess form whilst the meningitis is under treatment; (2) meningitis may be the result of leakage or rupture of a brain abscess; (3) meningitis may result in brain abscess (*see* page 155).

Early and adequate treatment of the meningitis and primary focus will reduce the likelihood of brain abscess developing simultaneously or subsequently. It is most important, however, to recognize the cases of meningitis which have a brain abscess as a primary focus. Sometimes, as for example in chronic aural infection, abscess is to be expected, but more usually persistent or increasing neurological defects following partial or complete recovery from the acute attack of meningitis or unexplained relapses will point to the diagnosis. Papilloedema, rising pressure of a cerebrospinal fluid which contains a few cells and an increasing amount of protein will be more suggestive. However, slight clinical disimprovement not reflected by gross changes in the cerebrospinal fluid, but, most significant of all, apathy and drowsiness, are urgent indications to search for abscess.

In this, the electroencephalogram has great value, for it is unlikely that a cerebral abscess will be present in the absence of slow delta activity focusing at or around the abscess site, and where such a focus exists a burr hole should be cut and a search made by cannula if there is the remotest possibility of suppuration within the brain. Treatment consists in frequent aspiration and the instillation of penicillin in high concentration (500,000 units in 1 millilitre), or other antibiotic if indicated by sensitivity tests. Progress is watched by means of Thorotrast pyograms. In certain circumstances the abscess should be excised, especially if aspiration is not proving satisfactory. Cerebellar abscesses usually give rise to unequivocal focal signs, but do not always do so, and in this group the observation that all is not well (apathy, drowsiness, unexplained earache or headache), fortified perhaps by the knowledge that at the time the mastoid was cleared there was diseased bone or extradural pus adjacent to the posterior fossa, will be the evidence on which the decision to explore the posterior fossa must be taken. Cannulation is difficult, a small abscess may be missed, and in the cerebellar fossa so difficult and perilous is the after-treatment of frequent aspirations that immediate excision of the abscess capsule provides the best results in most cases (Pennybacker, 1950; Botterell and Drake, 1952).

Foci of haematogenous spread

Blood-borne bacteria, arising especially of course from infections of the lung and chest wall, may cause meningitis which may be accompanied by brain abscess. Focal signs if dense and sudden in onset are clearly the result of an embolus; there has been no time for an abscess to develop and it may not do so if the organisms are sensitive to available antibiotics: however, watch must be kept during the next few weeks for evidence of raised pressure, of deterioration after partial recovery of the focal signs, and of changes in the electrical activity of the brain.

Treatment of the primary focus is not within the scope of this article, but an attack of meningitis may bring to light the existence of foci which require surgical treatment on their own merits.

SURGERY OF THE COMPLICATIONS

The sequelae of meningitis are related variously to the degree of neural damage at the entry point of the infection, the chronicity of the disease, the infecting organism, and the therapeutic agents employed. Early control of the invading organism, elimination of the primary focus and continuation of treatment for a sufficient period of time to prevent a relapse will, to a large extent, eliminate the complications. In this respect, control of infection is more important than duration of illness, for inadequately treated pneumococcal meningitis, albeit completely terminated within a few days, may have more serious sequelae than adequately controlled Gram-negative meningitis, although not completely eliminated for weeks.

Previously many of the cases of meningitis which recovered were tragic wrecks, including a large number of children who were mentally defective, epileptic, blind, deaf, hemiplegic or paraplegic. Amongst the less severely damaged might be found cranial nerve palsies or cauda equina lesions: there is little doubt that not a few of the latter were due to the intrathecal injection of either antimeningococcal serum which at that time was necessary and valuable, or solutions of sulphonamide drugs mistakenly. In other cases, loculation abscesses, subarachnoid cysts or progressive hydrocephalus provided problems, few of which could be solved. Complications are now less common, and advances in technique have made the successful treatment of some of them possible; only these will be discussed.

SURGERY OF THE CEREBRAL COMPLICATIONS

Loculation abscess

This is rare. During the acute phase of meningitis one of the deep extensions of the subarachnoid space into a sulcus may become *loculated and unless it resolves* by natural resistance or is sterilized by blood-borne antibiotics it may form an abscess, which by virtue of its position becomes intracerebral as it enlarges; such "sulcal" abscesses are *commonly associated with one or more deep loculi.* The infecting organism is not infrequently a streptococcus (Smith and her colleagues, 1946), which we have seen is also the commonest cause of subdural infection (Schiller, Cairns and *Russell, 1948), and these facts strongly suggest that the* abscess and meningitis may [illegible], perhaps a local suppurative thrombo- [illegible] ulation" occurs in meningitis there has [illegible] ogical signs, that it was present at the outset, lends further support to this concept. It is perhaps little realized that for some time meningitis may remain remarkably localized, being evidenced only by focal signs or convulsions, the almost normal cerebrospinal fluid giving a false indication of the severity of the disease. In fact, such a mode of onset may be more common than

is apparent, and would account for the occasionally severe and unexpected sequelae in a well-treated case. Diagnosis and treatment have been discussed.

Obstruction to cerebrospinal-fluid pathways

It has been established that the main stream of cerebrospinal fluid runs from the choroid plexus of the lateral ventricle to the absorptive areas over the cerebral hemispheres, and that obstruction at any level will eventually produce dilatation of all that part of the ventricular cavity or subarachnoid space rostral to the block: the secretion of fluid in other ventricles, other sources of fluid and scattered absorptive areas would not seem to compensate for an effective block of the main stream. Careful search for such a block naturally most likely to be found at one of the bottlenecks will meet with success in most cases (Russell, 1950), but where the hydrocephalus is extensive, confusion may arise, especially if the search is clinical, because of the development of secondary subarachnoid obstructions. These may occur in the acute stage as a result of brain herniations: (1) in either direction through the incisura of the tentorium or (2) down through the foramen magnum (Cairns, 1949) or may be produced when the infection has subsided as a result of the occupation of the cisterns at the incisura of the tentorium by hydrocephalic ventricles and their herniations. The observations of Dott and Levin (1936) and others that evidence of past inflammation is present in most cases of infantile hydrocephalus might justify consideration of nearly all the varied types of cerebrospinal-fluid loculation and obstruction as complications of meningitis, and indeed most examples of hydrocephalus have at some time or another been reported as following, perhaps years later, a clinical attack of meningitis. The commonest of these will be considered.

Internal hydrocephalus

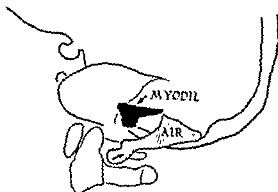
Internal hydrocephalus is rare as a late complication. Obstruction of a foramen of Monro, causing dilatation of one lateral ventricle (Dott, 1927) and of a temporal horn (Cairns and his colleagues, 1947), have been described following brain infections, but not following a clear-cut attack of pyogenic meningitis, although the latter has complicated tuberculous meningitis (Cairns, 1951). The main sites of obstruction are the iter of Sylvius and the foramina of Magendie and Luschka; the latter are more common and in fact are related intimately with and may not be distinguishable from subarachnoid adhesions in the posterior fossa.

Diagnosis.—Persistent headache, hydrocephalic attacks and papilloedema will suggest obstruction to the circulation of cerebrospinal fluid, but diagnosis can be accurately made only by careful ventricular studies. In most instances air studies will be satisfactory, but where pressure is very high or the ventricles large, a small quantity of Myodil, 1–2 millilitres, introduced into one lateral ventricle, may demonstrate the site of block with little disturbance to the patient and with none of the risks engendered by the pressure changes resulting from the use of air. In a certain number of cases there will be a mild or moderate meningeal reaction not severe enough to cause anxiety. Myodil is heavier than cerebrospinal fluid and moves slowly through the foramen of Monro, the long slender iter and the foramina of Magendie and Luschka: it outlines the narrow channels and reveals deformities and partial blocks not seen on air studies; when it is held up at the site of obstruction very useful further information can be obtained on occasion by the introduction of air from below (Fig. 86).

Treatment.—Ventriculostomy, that is opening the third ventricle into the surrounding subarachnoid space by the anterior or lateral routes, will provide immediate relief from any block distal to the third ventricle. However, this operation, at the outset so pleasing and satisfactory, may later fail because adhesions close the ostium, and this is very likely to happen where bulging ventricles have filled the subarachnoid space.

Torkildsen's operation, in which a rubber or Polythene tube is placed from the lateral ventricle into the cis[illegible]
and is th[illegible]
The tub[illegible]
into the subarachnoid space of the cisterna magna.

Block of one foramen of Monro is treated by making an opening in the septum pellucidum (Dott, 1927). Obstruction to one temporal horn may be cured by reopening the loculated part of the ventricle, and excision or destruction of the entrapped plexus (Cairns and his colleagues, 1947), or by laying a tube from it into the cisterna magna.





External hydrocephalus, and combined external and internal hydrocephalus

External hydrocephalus is more common and can result in the most serious rise of intracranial pressure. In many cases resolution occurs; perhaps necessarily aided by repeated lumbar punctures or by suboccipital or subtemporal decompression. On occasions the block persists and pressure rapidly builds up unless repeated daily lumbar taps are made and large amounts of fluid withdrawn. Dense adhesions are found along the brain base, sometimes covering the outlets from the fourth ventricle, and causing an internal hydrocephalus, most commonly closing the prepontine and ambient cisterns at the tentorial opening but occasionally extending anteriorly and closing the cisterna chiasmatis so completely that the carotid arteries and the circle of Willis are bound to the third ventricular wall by dense white adhesions. Although theoretically possible, evidence is rarely found (apart from subdural effusions) of profound exudate or organizing adhesions blocking the surface absorptive areas.

Diagnosis.—Diagnosis is not made readily; rather does the existence and site of a subarachnoid block gradually become evident as the result of (*a*) failure of a ventriculostomy or Torkildsen's operation to relieve symptoms in a known ventricular block, or (*b*) continued and severe raised intracranial pressure in the absence of ventricular block (as shown by a ventriculogram). This condition must be distinguished from the raised pressure of sinus thrombosis (Symonds, 1952), a condition which if not rapidly fatal by reason of thrombosis spreading in the cerebral veins, tends to recover spontaneously within a few weeks.

Treatment.—Lumbar punctures are useful in reducing pressure during the acute phase. In the absence of electroencephalographic changes suggestive of a cerebral abscess, severe papilloedema and visual failure may lead the surgeon to make a suboccipital decompression to save vision and search for a cerebellar abscess. There may be progressive increase in the size of the bulge (Fig. 87) and no relief from papilloedema unless daily lumbar punctures or aspirations of the decompression are carried out. In such cases replacement of some of the fluid in the decompression by air will safely demonstrate radiologically whether or not the pressure is due to a block at the tentorium or whether there is in addition a ventricular block. If no air enters the

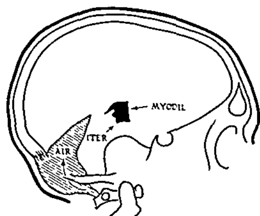
ventricular system a small quantity of Myodil introduced through a burr hole may demonstrate the level of ventricular obstruction (Fig. 88).

A certain number of mild cases respond to subtemporal or suboccipital decompression which rapidly relieves the symptoms, but which continues to bulge for many months as evidence of its necessity.



Fig. 87.—Post-meningitic hydrocephalus. Tense bulging of occipital decompression performed urgently to save vision It was necessary to aspirate this daily to prevent headache and vomiting Cure followed intubation of cisterna ambiens

It is quite clear that Torkildsen's operation and ventriculostomy of the third ventricle are of no avail where subarachnoid pathways are closed.



Fi[illegible] 88 [illegible] Post-men[illegible] hydrocephal[illegible] [illegible] ways, nor can it enter the ventricular system.

Intubation of the cisterna ambiens is another recognized method of treatment. Traversing the tentorial incisura are the narrow subarachnoid pathways which connect the great lakes above and below. These are readily obliterated by exudates which organize to form dense adhesions, the resulting tentorial block providing one

of the great problems in recovered meningitis. The [illegible] and a blocked cisterna ambiens cannot be [illegible] happens that in many cases in which den [illegible] chiasmatis and anterior end of the ambiens remain patent, inviting a short circuit to the open cisterns above the *tentorium. Division* of the tentorium and opening up the patent anterior extremity of cisterna ambiens has not proved successful, so as an experiment a tube was placed from the lateral ventricle across the upper surface of the tentorium and threaded into the anterior end of cisterna ambiens (Fig. 89). This has proved successful in cases where a patent subarachnoid space could be found in front of the dense adhesions at the tentorial opening [illegible] of choice where the forami [illegible] opening may be made in the [illegible] over, where the ventricle is very large it produces a secondary block of the subarachnoid pathways at the tentorial opening.

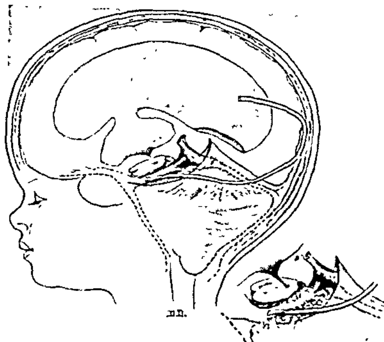


FIG. 89.—Intubation of cisterna ambiens. Ventriculo-cisternostomy. Diagram of post-meningitic hydrocephalus; the mid-brain has been cut across at tentorial level to show a stricture of the iter and an arachnoidal block at the tentorial incisura which prevents success of the Torkildsen operation. A tube from the lateral ventricle rests on the upper surface of the tentorium and is threaded into the anterior end of the cisterna ambiens. This must be placed well into the subarachnoid space anterior to the adhesions (see inset).

Subarachnoid loculation

Although there is no doubt that loculi of small size are often present during the course of acute meningitis, and may be encountered when searching for a brain abscess, they rarely persist and cause trouble when the infection has passed. Solitary arachnoid cysts which burrow into the brain, causing raised pressure and severe disabilities, are well known, but it is not at all clear that they follow meningitis.

Treatment.—Simple excision of the outer (arachnoid) membrane is followed by reformation of the cyst. Cure can be effected only by (1) making a wide opening into a ventricle, or (2) laying a tube from the cyst to a ventricle or one of the large subarachnoid cisterns.

TREATMENT OF THE SPINAL COMPLICATIONS

Loculation of pus

This has been described (*see Case II*), and may possibly occur at the portal of entry of infection in some cases, for example congenital spinal dermal sinus. It is certainly true that loculation occurs early in the disease.

Diagnosis may be suggested by the neurological signs, and in a few cases will be dramatically confirmed by the entry of the loculus by the lumbar puncture needle.

Treatment is that of the meningitis, but in retrospect there would perhaps be a case for laminectomy and drainage of the infected loculus, if diagnosed early and before infection has spread too widely and deeply.

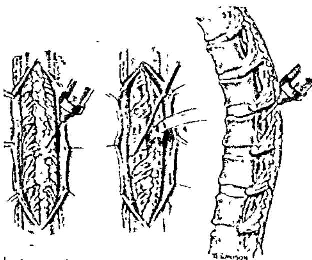
Spinal arachnoiditis and loculation of the cerebrospinal fluid

Encysted collections of cerebrospinal fluid are known to follow meningococcal meningitis, especially those cases treated with intrathecal anti-meningococcal serum, and tend to cause progressive spinal-cord compression. This is illustrated by the following case of meningitis occurring 20 years ago.

CASE VII.—L. R., aged 7 years. Cerebrospinal meningitis, recovery; spinal-cord compression by subarachnoid loculi (Sir Geoffrey Jefferson's case).

Four years before, this little boy had been playing normally outside, when he was

FIG 90 —Spinal arachnoiditis; loculi following cerebrospinal meningitis (*Case VII*). Laminectomy exposes a thin cord displaced backwards by anteriorly placed arachnoidal cysts. An area of scarring on the dorsum of the cord was aspirated by means of a fine needle, and by this means the cysts anterior to the cord were first located. Treatment was by partial excision and aspiration (Sir Geoffrey Jefferson's case)



taken acutely ill, and within a few hours was almost moribund from meningococcal meningitis. He was treated with polyvalent anti-meningococcal serum; intramuscularly, intravenously, and on 11 occasions intrathecally For a month he hovered between life and death. [illegible]

spinal fluid. He was to recover eventually, some 6 months after the onset, and could see and walk, although a drop foot remained permanently: a poor result by modern standards, but he recovered from a disease more difficult to eradicate at that time than tuberculous meningitis now. The anti-meningococcal serum, although so feebly active, represented the only advance in treatment during 100 years, apart from the gradual discarding of cupping, blistering and bleeding. He developed normally until 7 weeks before admission when his legs became weak, and within a short time were paralysed. A complete block with a Froin's syndrome was found on lumbar puncture, and at operation an anteriorly placed multilocular cyst was exposed and partly excised (Fig. 90). The length of cord compressed was such that three separate laminectomies were required to complete the operation. Improvement was only slight, as was expected by evidence of inflammatory changes in the cord itself seen at operation.

It is clear that there is no cure for spinal arachnoiditis, for simple removal of part of the arachnoid membrane is followed by re-formation as healing occurs, and relapse of the compression. It offers even greater difficulties than cerebral arachnoiditis.

Radiculitis and pain

Permanent damage to nerve roots may result in considerable disablement, for example in dropped foot, trophic ulceration, sphincter disturbances or persistent pain. It should be emphasized that the fibrosis which envelops the cauda equina is not produced by lumbar puncture, but is due to early loculation, prolonged infection, or the injection of irritants such as soluble sulphonamides.

Treatment

Orthopaedic procedures are indicated in certain palsies and deformities.

Sympathectomy will improve trophic ulceration and erythrocyanosis.

Cordotomy, usually upper dorsal, is of extreme value in curing persistent pain. Local operations on nerve roots have been proved to be valueless.

CONCLUSION

The incidence of meningitis has fallen with improved care of adjacent infections, especially aural disease, and better diagnosis and treatment of the more obscure primary foci. Great strides have been made in the control of the acute disease with antibiotics, and further progress will be made as a result of the study of antibiotic action and the biochemistry of bacterial growth. It should be remembered, however, that in spite of an effective anti-bacterial armamentarium, the pneumococcus, for example, may strike so suddenly that death may occur before therapy can be effective. Improved prognosis in meningitis in adults has not been followed so closely in infants: there are several factors here; less resistance to infection, more difficulty in diagnosis, and greater problems in treatment, including intravenous therapy and the administration of intrathecal antibiotics, with a narrower margin between effective and dangerous dosage. For this reason systemic antibiotics finding their way into cerebrospinal fluid have great value, but until and unless the local concentration can be reached as quickly and as effectively as it can by intrathecal administration, such drugs should be used only exclusively in the less severely ill cases; the choice will often be a nice one.

(*See also British Surgical Practice:* Meninges—Meningitis, Acute and Chronic, Vol. 6, page 69, S Key 233.)

REFERENCES

Ainley-Walker, K. M. S., and Bosanquet, F. D. (1952) *Lancet*, 1, 433.
Alexander, G. L. (1949). In *British Surgical Practice*. Ed. by Sir Ernest Rock Carling and Sir James Paterson Ross. Vol 6, p. 69. London: Butterworth.
[illegible] *[illegible] in Pediatrics*. Vol 5, p. 273. Ed. by Levine. Chicago.

Gibson, Count Dillon, and James, D. G. (1952). *Lancet*, 2, 1203.
Hoyne, A. L. (1948). *Ill. med. J.*, 93, 255.
Hoyne, A. L., and Riff, E. R. (1951). *J. Pediat.*, 39, 151.
Jackson, Ina (1949). *Arch. Neurol. Psychiat.*, 62, 572.
Jawetz, E., and Gunnison, L B. (1952). *Antibiotics Chemotherapy*, 2, 243.
Jefferson, G (1950). Macewen Memorial Lecture, 1948. Jackson; Glasgow.
Johnson, R. T. (1947). *Brit. J. Surg.*, War Surgery Supplement No. 1, p 172.
— and Dick, R. C. S. (1945) *Lancet*, 2, 193.
— and Dutt, P. (1947) *Brit. J. Surg*, War Surgery Supplement No. 1, p. 141 (1953).
Jones, H. E. (1952). *Lancet*, 1, 891.
Lepper, M. H., and Dowling, H. F. (1951). *Arch. intern. Med*, 88, 489.
Levinson, A., Luhan, J A., Mavrelis, W. P, and Herzon, H. (1950). *J. Neuropath*, 9, 406.
Logue, V. (1951). *Modern Trends in Neurology*, p 363. London; Butterworth
— and Till, K. (1952). *J. Neurol. Neurosurg. Psychiat*, 15, 1.
Lorber, J. (1951) *Arch. Dis Childh*, 26, 28.
Matson, D. D, and Ingraham, F. D. (1951) *Pediatrics*, 8, 463.
Monro, Alexander (1887). *Anatomy of the Brain* Vol. 1. Hydrocephalus Edinburgh; Maclachlan and Stewart.

Office.

Schiller, F., Cairns, H., and Russell, Dorothy S. (1948). *J Neurol. Psychiat.*, 11, 143.
Smith, Honor V (1951) *Practitioner*, 166, 334.
— Duthie, E. S, and Cairns, H. (1946). *Lancet*, 1, 185.
— and Vollum, R. L (1950). *Lancet*, 2, 275.
Spitz, E., Pollak, A, and Angrist, A. (1946) *Arch Neurol. Psychiat.*, 53, 144.

CARDIOSPASM

By P. R. ALLISON, B.Sc., M.B., Ch.M., F.R.C.S.
Thoracic Surgeon to the United Leeds Hospitals

AETIOLOGY

It must be acknowledged that the aetiology of cardiospasm is not known, even though many explanations have been offered. Some would assert that it is not a disease in itself but a manifestation of different disorders, and that both the aetiology and pathology of these vary, even though they produce a radiological and clinical picture common to them all. In order to assess the value of some of these suggestions it is necessary to remember that cardiospasm is a progressive condition with varied secondary changes, and that the finding of different secondary manifestations in two patients does not necessarily imply that the primary lesion is different as well. Thus, for example, the finding of degeneration of Auerbach's plexus in one oesophagus and [illegible] examination of the bronchial tree would show no abnormality, whereas in the later stages bronchitis, emphysema, and degeneration of bronchial elements may be found as well as more distant changes in the heart and pulmonary vessels.

There is no doubt that the oesophagus is subject to various neuromuscular disturbances which bear no resemblance to cardiospasm, except in so far as they cause dysphagia. In the present state of knowledge it is better to regard cardiospasm as a single entity which may be encountered clinically in various stages of development, and with varied secondary changes. As a result of a suggestion that cardiospasm is not, in fact, a spasm but a failure of the cardia to relax, the word achalasia was coined, and received much support, but the evidence in favour of this is as flimsy as that for any other of the many explanations given, and at present it appears to have no great virtue. Cardiospasm and achalasia must be accepted as synonyms for a single disorder. Some, those who object to the term cardiospasm, point to the absence of thickening of the circular muscle fibres of the oesophagus at the cardia to produce a sphincter, but it is obviously unnecessary to presuppose a sphincter for spasm, as it can be observed in the bronchial tree or the intestine, where no special muscular development exists. That cardiospasm was really a failure to relax before the peristaltic wave was linked with the finding of degeneration of Auerbach's plexus and the absence of ganglion cells in the lower oesophagus in advanced lesions, but most workers now agree that such changes are an effect and not a cause.

A further suggestion that cardiospasm was not intrinsic, but caused by the dia- [illegible] that there is no [illegible] about abnormal action are confused, and often contradictory. [illegible] interpretation of cardiospasm, and the one strongly favoured by the author, is that it is an expression of psychosomatic disharmony. From time to time, many examples have been quoted of people developing dysphagia after a "nervous shock", and many more have supported an opposite view by relating patients in whom no such upset occurred. These arguments are not really relevant, for the outcropping of an obvious symptom like dysphagia does not need a single dramatic nervous experience for its explanation, but may be the result of deep conflicts of which the patient himself may

be only dimly aware. That established cardiospasm does not react favourably to psychotherapy is undoubtedly true, but this again cannot be accepted as important in the discussion of aetiology, for cardiospasm at the stage at which it presents for treatment is to the oesophagus what bronchitis, fibrosis and emphysema is to the lungs in asthma; few would deny that asthma is a psychosomatic disorder, and few would expect psychotherapy to be very effective in the treatment of this late stage.

A further parallel can be drawn between asthma and cardiospasm. Normal breathing depends on an accurate co-ordination between the unstriped muscle of the bronchial tree and the striped muscles of respiration. In the same way normal passage through the cardia depends upon co-ordination between the striped muscle of the diaphragm and the unstriped fibres of the oesophagus and stomach. Such delicately balanced systems could obviously be upset very easily, and it is suggested that this may in fact take place as a result of emotional conflicts. The slang phrase in relation to a situation "I cannot swallow that" may have more significance than is generally attached to it.

Psychological factors

There has been much argument about psychological factors in the aetiology of cardiospasm. The upset seems to have a distinctly psychosomatic basis, and although psychiatric treatment alone does not cure the established disorder, this side of the problem must never be neglected It is not enough to diagnose cardiospasm in a hurried outpatient clinic, and arrange for the appropriate organic treatment. Half an hour apart with the patient in private will disclose important worries that may be connected, such as a fear of cancer of the throat arising from association with a relative or friend dying from such disease. Although the onset of symptoms may be too buried in the past for a surgeon to unearth, occasionally they date from an obvious state of tension. A young man returning from prison camp takes an insecure job, marries, a baby arrives, and then the sudden death of his mother occasions the onset of dysphagia. Such histories can often be elicited, and much help can be given in relieving the contributory tensions.

THE PHYSIOLOGY OF THE CARDIA

It has already been said that the method of action of the cardia is not agreed upon. It is therefore fruitless to describe the different explanations that have been offered, from time to time, of how the cardia allows the passage of food into the stomach, while preventing its reflux into the oesophagus in all but the abnormal circumstances of belching and vomiting. Clinical, radiological, oesophagoscopic and operative experience of a variety of diseases and disorders of the cardia all suggest that its normal action depends not upon one thing but on a number of factors which are closely co-ordinated. A discussion of all the evidence on which such a conclusion is based would be out of place in this article, but the following conception will make it [illegible]

[illegible]

stomach, and increases this in inspiration. The left lobe of the liver may play some part in this extrinsic mechanism inasmuch as it forms a buttress to the anterior wall of the lower oesophagus.

PATHOLOGY

It is not often possible to obtain a post-mortem examination of the oesophagus from a patient with very early cardiospasm, but such examinations as have been made show neither macroscopic nor microscopic change at any level. This is in accord with the conception of a functional disturbance. Both radiological and operative findings in the established disorder confirm that the obstruction is in the lowest 1–1·5 centimetres of the oesophagus, which is normally that part within the grip of the right crus of the diaphragm. Where the cardia prolapses into the abdomen, as it may do for some distance in cardiospasm, the obstruction is still found in the same place immediately above the stomach, not related to the diaphragm. At operation this area is cylindrical on section, and contracted so that it feels more like solid muscle without lumen, but there is no fibrosis, no hypertrophy of muscle and no rigidity. The mucous membrane on the inside is normal. The area of contraction is never visible in the mediastinum when the oesophagus is viewed from the chest, but it can easily be brought into view by traction. The oesophagus above this area is dilated and the muscle wall thickened. In the later stages there may be increased fibrous tissue in the muscle wall, and the ganglion cells of Auerbach's plexus may disappear. The mucous membrane of the dilated oesophagus is usually surprisingly clean, but in some patients thickening of the mucosa and even severe ulceration may occur.

The oesophagus not only dilates, but also elongates. As this happens it becomes tortuous or sigmoid It then usually projects mainly into the right side of the chest with a small secondary curve to the left at the lower end, but occasionally the main deformity may be to the left. The weight of the oesophagus may cause it to prolapse through the hiatus of the diaphragm into the abdomen for as much as 3 or 4 inches. Very rarely a cardiospasm may be associated with herniation of the stomach upward into the mediastinum through the hiatus. The occurrence of these last two abnormalities make it certain that the diaphragm is not the primary cause of the obstruction.

Secondary changes may be found in the lungs either from spill and inhalation, from pressure of the dilated oesophagus on the bronchus, or from a combination of these. Even in the absence of chronic pulmonary changes, but in the presence of secondary oesophagitis, the changes characteristic of rheumatoid arthritis may be present. The general condition of the tissues of the body may vary from normal to extreme emaciation.

CLINICAL FEATURES

Age considerations

Cardiospasm may occur at any age and in either sex. It has been seen in a child as young as 4 months, and in an adult as late as 72 years. It may cause severe and distressing symptoms or the patient may be unaware of any abnormality. The symptoms when present may be intermittent or continuous. The patient's nutrition may be normal, or there may be progressive emaciation and death from starvation. It would seem that a child who has had cardiospasm from a very early age may not know what normal swallowing should be, and therefore may not complain about any difficulty.

Hydrostatic pressure

The oesophagus dilates above the obstruction, and may be able to hold a fairly large meal which then passes slowly through the cardia into the stomach as a drip feed by its own hydrostatic pressure. There is normally in the oesophagus a negative pressure related to the general intrathoracic pressure while the pressure in the abdomen and stomach is positive. The mechanism at the cardia normally relaxes easily, and there is only need for a small head of pressure to drive the food into the stomach.

This is provided partly by hydrostatic pressure and partly by the force of the oesophageal peristaltic wave. In cardiospasm greater pressure is required to relax the cardia, and at the same time the muscular movements of the oesophagus above are less co-ordinated. Movement of food is therefore likely to be by an increased hydrostatic pressure. Thus it happens that there may be a persistent fluid level in the oesophagus.

Maintenance of nutrition

The constant drip of food into the stomach, so long as its hydrostatic pressure in the oesophagus is great enough to overcome the contraction of the cardia, explains why most patients maintain a good nutrition. It may also explain why patients will complain that food meets an obstruction higher in the chest than the cardia, for the site of obstruction feels to be at the level at which the bolus reaches the persistent fluid level. In fact patients reach a stage of equilibrium where, instead of storing their meal in the stomach and passing it along a little at a time into the duodenum, they store it in a dilated oesophagus and pass it slowly into the stomach. From the metabolic point of view, there is no great difference between the two processes.

Dysphagia

The main symptom then is usually dysphagia. Although it is very unwise to attempt to make a diagnosis of the cause of dysphagia from the clinical description, it is well to recognize the variety of descriptions that exist with a common pathology. Food may lodge at the lower end of the sternum, and may cause discomfort or even quite severe pain. The obstruction may persist so that in the early stages the patient may have to retch to bring the food back, or he may suddenly feel the cardia relax, and the bolus enter the stomach. Whether he brings the bolus back or it passes on, the rest of the meal may then be taken in relative comfort. The more intelligent patients may develop means to help overcome the obstruction. As already stated, when the oesophagus is very dilated with a persistent large residue, the obstruction may be referred to a higher level, sometimes even the root of the neck. The dysphagia is nearly always increased by nervous tension or apprehension so that it is usually worse when the patient is dining out than when he is alone and at home. One sufferer was known always to book a table for two in a corner when he had to eat in a restaurant, so that he could put up the newspaper to shield him from observation, and carry out, without embarrassment, the antics that helped him to swallow his food. Sometimes solids may be taken better than fluids, and sometimes the reverse is the case. Warm things usually pass better than cold, but many of the differences that occur can only be explained on the basis of association and functional disturbance, for a patient may aver that coffee goes down better than tea, or that beef goes down better than mutton, and so on.

As already stated, some patients may deny any dysphagia, and it is believed that they have had the obstruction since such early childhood, that they have never known anything other than their own form of ingestion, which they accept as normal. They may seek advice about bronchitis, or even rheumatism, or the abnormal mediastinal shadow may be noticed during mass radiological survey. The occurrence of this group has led some authors to describe mega-oesophagus as a separate entity from cardiospasm, but there is no justification for this. On detailed investigation they are found to differ in no way from the more usual form of cardiospasm, with dysphagia.

Loss of weight

Loss of weight is variable. The commonest history is of loss of 1–1½ stones in the early months of the disorder, followed by maintenance of weight and nutrition on the new level indefinitely. Some patients, however, do not lose weight, and occasionally some will starve to death. Such variations still further emphasize the functional nature of the complaint.



(a)



(b)



(c)

FIG. 91 (a), (b) and (c).—Skiagrams showing development over a 3-year period.

Regurgitation and vomiting

When present, regurgitation and vomiting are usually self-induced to relieve fullness in the chest, pain or obstruction. Often a patient will know that if he can partly fill his oesophagus, leave the table and induce vomiting, he may then be sure of being able to finish his meal in comfort. The crico-pharyngeal sphincter usually remains competent in cardiospasm, but it may become relaxed during sleep, when oesophageal contents may flow back into the pharynx. This may drool out on to the pillow, it may wake the patient choking, or it may be inhaled into the lungs.



FIG 92—The second stage of cardiospasm with dilatation and exaggerated but incoordinated movements.



FIG 93—The third stage of cardiospasm where the movements have disappeared and the oesophagus has become an inert bag.



FIG 94—Skiagram of patient with proved cardiospasm showing normal gas bubble in the stomach

Pulmonary symptoms

Usually the oesophageal contents are irritating enough to stimulate the cough reflex, but this may be taken off guard, or, if liquid paraffin has been taken with the object of easing the passage of a meal through the cardia, this may seep into the lungs without stimulating the cough or waking the patient. Thus it happens that pulmonary complications are not very uncommon, and may in fact be the cause of the presenting symptoms. Shortness of breath, cough and recurrent febrile bouts may occur. These



(a)



(b)



(c)

FIG 91 (a), (b) and (c).—Skiagrams showing development over a 3-year period.

Regurgitation and vomiting

When present, regurgitation and vomiting are usually self-induced to relieve fullness in the chest, pain or obstruction. Often a patient will know that if he can partly fill his oesophagus, leave the table and induce vomiting, he may then be sure of being able to finish his meal in comfort. The crico-pharyngeal sphincter usually remains competent in cardiospasm, but it may become relaxed during sleep, when oesophageal contents may flow back into the pharynx. This may drool out on to the pillow, it may wake the patient choking, or it may be inhaled into the lungs.



FIG. 92.—The second stage of cardiospasm with dilatation and exaggerated but incoordinated movements

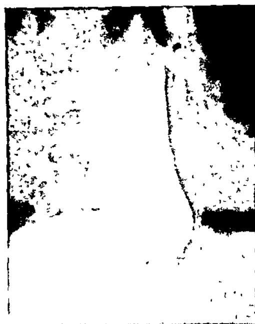


FIG. 93.—The third stage of cardiospasm where the movements have disappeared and the oesophagus has become an inert bag



FIG. 94.—Skiagram of patient with proved cardiospasm showing normal gas bubble in the stomach.

Pulmonary symptoms

Usually the oesophageal contents are irritating enough to stimulate the cough reflex, but this may be taken off guard, or, if liquid paraffin has been taken with the object of easing the passage of a meal through the cardia, this may seep into the lungs without stimulating the cough or waking the patient. Thus it happens that pulmonary complications are not very uncommon, and may in fact be the cause of the presenting symptoms. Shortness of breath, cough and recurrent febrile bouts may occur. These

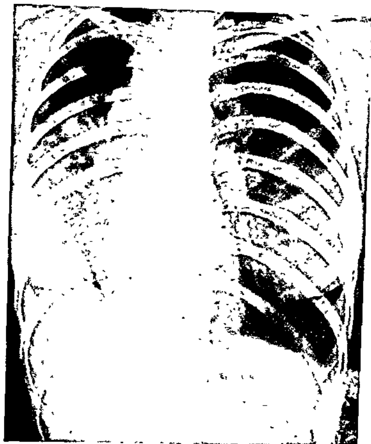


FIG. 95.—Skiagram of chest of patient with cardiospasm showing dilated oesophagus projecting into right chest. Note secondary *pulmonary* complication.

may go on for years, being regarded by the patient as recurrent bronchitis. They may cause clubbing of the fingers and arthritic changes before the true nature of the trouble is suspected. More severe *respiratory illnesses may give physical signs of* pneumonia or pulmonary collapse. All these may be the result of inhalation alone, but occasionally it may happen that a huge oesophagus may compress a bronchus, and so predispose to obstructive collapse.

RADIOLOGICAL APPEARANCES

The well-established and classical picture of cardiospasm is of a sinuous, inert and [illegible] stenosis at the cardia. The tendency [illegible] own that the [illegible] In the earlier *stages the lower two-thirds of the oesophagus may appear contracted with a little* relative dilatation of the upper third (Figs. 91*a*, *b* and *c*). The movements of the segment below the aortic arch may be exaggerated but incoordinated, and normal peristalsis may not be seen. After a variable time this length of oesophagus begins to dilate, except at the cardia, but vigorous incoordinated movements persist (Fig. 92). As the dilatation increases the movements gradually become less until finally the oesophagus becomes an inert bag (Fig. 93). The smooth funnel-shaped narrowing at the lower end is present throughout. Often no gas bubble is to be seen in the fundus of the stomach, but although this may be an interesting radiological point of differential diagnosis, too much reliance must not be placed upon it, for it is not constant (Fig. 94). It has already been noted that as the oesophagus dilates it tends to project *to the right, causing a soft tissue shadow down the right side of the mediastinum* which has sometimes been mistaken for tumour or massed glands (Fig. 95). Occasionally the dilated oesophagus may project to the left, forming a large shadow here (Fig. 96).



FIG. 96.—Dilated oesophagus in cardiospasm projecting into left side of chest.



FIG 97.—Lower oesophagus prolapsed through the hiatus into the abdomen in a case of cardiospasm.



FIG. 98.—Cardiospasm associated with para-oesophageal hiatal hernia.



FIG. 99.—Cardiospasm without much general dilatation of the oesophagus, but with local dilatation to the left forming diverticulum.

Pictures in the upright position may show a fluid level in the oesophagus. If the cardia prolapses into the abdomen (Fig. 97), it still remains contracted. In the recumbent position a gas bubble may then be seen below the diaphragm, but this is in the oesophagus and not in the stomach. One example of cardiospasm associated with a hiatal hernia of the stomach has been seen, but this must be very rare (Fig. 98). In one patient there was very little general dilatation of the oesophagus, but a large local dilatation like a diverticulum was found projecting to the left above the hiatus (Fig. 99).

OESOPHAGOSCOPIC APPEARANCES

Oesophagoscopy should never be performed on these patients without a preliminary oesophageal wash-out. It is almost impossible to clean out a dilated inert oesophagus by siphonage alone and strong suction should be available. Even after this there is usually some fluid and food residues to be aspirated during oesophagoscopy, and it is wise to have reserve suction tubes available to avoid the danger of inhalation during anaesthesia. The oesophagus is found to be dilated to a variable degree according to the stage of the disorder, but the mucous membrane is usually and most surprisingly of normal appearance. When stagnation has been present for a long time, the mucosa may be a little thickened and unhealthy, and sometimes severe ulceration is seen. The cardia relaxes easily to the passage of the instrument and its walls are felt to be soft. This is an important point in the differential diagnosis of cardiospasm and carcinoma of the stomach invading the lower oesophagus from without, for in the latter condition the cardia may look just the same but is firm or hard on contact with the oesophagoscope or bougie.

TREATMENT

The relief of dysphagia from cardiospasm is so simple and so effective that there is no justification for the incomplete palliation of drugs and bougies. Hurst's mercury bougie has been a valuable form of treatment in the past, but it is now long out of date. Octyl nitrite will sometimes relieve the immediate discomfort of obstruction in the early stages of the disorder, but it must only be considered as a temporary expedient.

The surgical management of these patients has been confused, and to a certain extent discredited, by the elaboration of complicated operative procedures such as oesophagogastrostomy, cardioplasty, and excision of the cardia which have been associated with a high mortality, and complications worse than the original complaint. Modern treatment is limited to two methods of approach: (1) stretching the cardia; and (2) operative division of the muscle at the lower end of the oesophagus which is variously known as oesophageal myotomy or Heller's operation. Any method of treatment should be immediately preceded by oesophageal wash-out and suction aspiration, as the administration of a general anaesthetic to a patient with a dilated oesophagus full of food residues is fraught with danger of drowning, suffocation or aspiration broncho-pneumonia.

Digital dilatation of the cardia

For those who are not practised in the use of the oesophagoscope, stretching of the cardia is probably most safely performed by laparotomy, gastrotomy and digital dilatation. First the index finger is passed through the cardia, then two fingers, three, and finally four. The results of such dilatation gently performed are good. If severe oesophageal ulceration is present, there is an obvious risk of mediastinitis, and such [illegible] have been reported in the past. The combination of oesophageal toilet [illegible] ns. From [illegible] igoscopy [illegible]

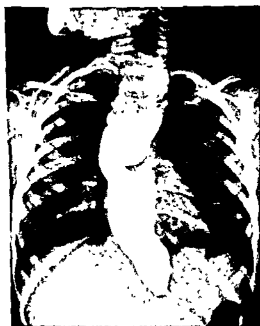


(a)



(b)

FIG. 100 (a) and (b).—Skiagrams of oesophagus in patient with cardiospasm before and after dilatation with the Negus hydrostatic bag



(a)



(b)

FIG. 101 (a) and (b).—Cardiospasm in a child aged three years before and after Heller's operation.



(a)

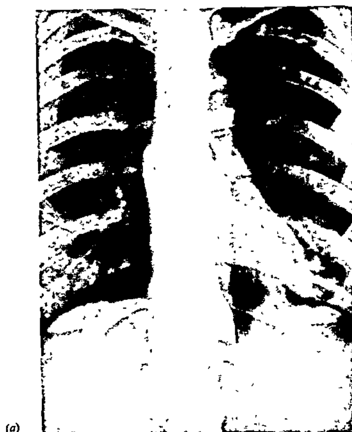


(b)

Fig. 102.—Cardiospasm with prolapse into the abdomen. (a) Before treatment. (b) After Heller's operation combined with repair of the hiatus and the ligaments of the cardia.



Fig. 103.—Lung abscess complicating cardiospasm.


(a)

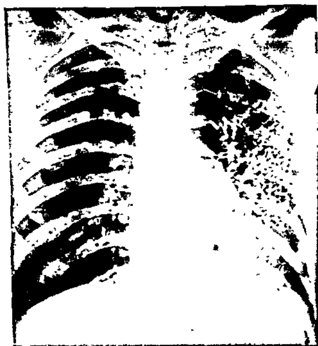

(b)

FIG. 104 (a) and (b).—Cardiospasm complicated by collapse and bronchiectasis of the left lower lobe and lingula.



Fig. 105.—Extensive bilateral chronic inhalation pneumonia *developing into* bronchiectasis complicating cardiospasm.



Fig 106.—Extensive carcinoma of middle third of oesophagus occurring *six years after successful* treatment of cardiospasm by Heller's operation.

and dilatation by some form of hydrostatic bag, as this can be performed on an out-patient and obviates an abdominal operation. Various forms of dilater have been devised. The principles of the best ones are that they are distended with water so as to produce even stretching, and that they have incorporated in them a pleated bag which cannot be over-distended. The use of jointed metal dilaters is more dangerous inasmuch as they are more liable to tear the mucous membrane. The hydrostatic bag favoured by the author is that devised by Negus. The careful use of this instrument,

perhaps repeated once or twice, has been found to give long-standing symptomatic relief and radiological improvement in about 60 per cent of patients (Fig. 100*a* and *b*).

Heller's operation

Heller's operation is reserved mainly for three classes of patients: (1) those who do not respond to dilatation; (2) those in whom the oesophagus is too tortuous for the cardia to be seen through the oesophagoscope; and (3) children (Fig. 101*a* and *b*). The operation consists of a longitudinal incision one inch long through the muscle at the extreme lower end of the oesophagus, the incision passing over on to the stomach so that the oesophageal and gastric mucosa bulge freely. It is essential that the line of the cardia should be transgressed and that any constricting bands in the submucosa should be divided. A small vein at the cardia is usually encountered and should be ligated. This operation may be performed by thoracotomy or by laparotomy. Those who have tried both ways mostly agree that the approach through the left pleural cavity gives the best exposure for accurate division of the muscle. If the hiatus is very lax, or if the cardia has prolapsed into the abdomen, the ligaments of the cardia should be repaired and the hiatus reduced as in the operation for hernia, because otherwise reflux oesophagitis may occur (Fig. 102*a* and *b*).

After operation clear fluids are given for 24 hours, followed by soft foods for a day or two and then a normal diet. Heller's operation, performed with accuracy, is so effective that relief can almost be guaranteed and it has the further great advantage that it does not produce incompetence of the cardia.

COMPLICATIONS

Complications from reflux and inhalation of oesophageal contents have already been mentioned. Recurrent bronchial attacks, pneumonia, lung abscess (Fig. 103), lobar collapse (Fig. 104*a* and *b*) and bronchiectasis (Fig. 105) have all been observed. Where liquid paraffin has been taken, inhalation of this relatively non-irritating substance is even more likely and paraffin pneumonia has been described. Oesophagitis with extensive ulceration sometimes occurs and is more likely in those patients who have used the Hurst's tube for many years. It is fortunately much less common than might be expected. Carcinoma of the oesophagus complicating long-standing cardiospasm has been observed in 4 per cent of the author's series (Fig. 106).

Perforation of the oesophagus with mediastinitis or pyopneumothorax or even peritonitis may occur as a result of instrumentation performed either by the patient himself or by his doctor. Subacute perforation may be treated expectantly with oesophageal hygiene, intravenous feeding and antibiotics, but acute perforation calls for immediate surgical repair. It is important to be certain about the level of perforation before attempting repair, and this can be done by a Lipiodol swallow, x-ray screening and oesophagoscopy. It is never wise to accept the account of some other surgeon who claims to have perforated the oesophagus at a particular level. Whether perforation is in the neck or the chest the results of immediate repair are good, but the operation should be accompanied by relief of the obstruction by Heller's operation. If this is carried out, it is not necessary to perform a gastrostomy, as fluid feeding can be started very soon

(*See also British Surgical Practice* Oesophagus, Vol. 6, page 314, S Key 247.)

FRACTURES OF THE PELVIS

By F. W. HOLDSWORTH, M.Chir., F.R.C.S.
Orthopaedic Surgeon, Royal Infirmary, Sheffield

The pelvis consists of the two innominate bones and the sacrum. The innominate bones articulate with the sacrum behind at the sacro-iliac joints and with each other in front at the symphysis pubis and thus form the pelvic ring. This ring is extremely strong and serves as a firm base for the spine.

Fractures of the pelvis may be divided into four groups: (1) avulsion fractures due to muscle action; (2) fractures of the pelvic ring; (3) fractures of the sacrum and coccyx; and (4) fractures of the acetabulum.

AVULSION FRACTURES

Avulsion fractures are most common in adolescence and result from forcible muscle action usually whilst playing games. The commonest of these injuries is avulsion of the anterior superior spine (Fig. 107) due to sudden action of the sartorius. Sudden contraction of the rectus femoris may avulse the anterior inferior spine; or of the hamstrings, the epiphysis of the ischium. All these injuries are easily diagnosed and all should be treated conservatively by rest in bed with the leg supported in the most comfortable position on pillows for 3–4 weeks followed by exercise. Recovery is complete in 6–8 weeks.

FRACTURES AND DISLOCATIONS OF THE PELVIC RING

Fractures of the anterior part of the ring

Division of the pelvic ring at one site does not result in displacement, for the ring is rigid and division in one place does not disturb the position of the ring as a whole. The commonest single injury is unilateral fracture of the pubic rami. Displacement is always slight and the only treatment necessary is rest in bed for 3–4 weeks. Full recovery occurs in about three months. Even if there are two fractures of the pubis isolating one fragment of bone the displacement is unimportant and the treatment is as for a single fracture (Fig. 108)

Fracture of the win [illegible] occurs with some frequency (Fig. 109). [illegible] displacement may occ[illegible] for the ring is intact. [illegible] exercises is all that is necessary. The prognosis is excellent.

Subluxation of the sacro-iliac joint

Occasionally subluxation of the sacro-iliac joint occurs as the result of torsional violence. The displacement is minimal and cannot be detected by x-ray examination. The affected region of the sacro-iliac joint is extremely painful and tender, and careful palpation may reveal asymmetry of the posterior superior iliac spines. In such cases straight leg raising on the affected side causes severe pain in the sacro-iliac joint.

The displacement should be reduced by manipulation. The patient lies on the sound side and the ilium on the affected side is rotated forwards, counter-pressure being maintained upon the shoulder. Following reduction, the spine and pelvis are immobilized



FIG. 107.—Avulsion of the anterior superior spine.

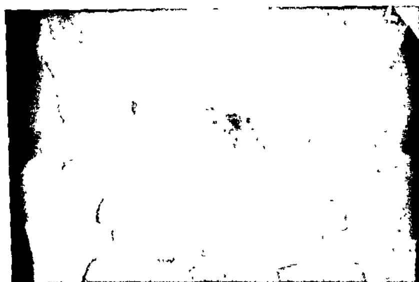


FIG. 108.—Fractures of the pubic rami on *both sides* The posterior part of the pelvic ring is stable.

in a plaster jacket for 8–10 weeks to prevent recurrence of the torsional displacement. In spite of reduction and immobilization, however, the joint frequently remains painful. The pain is probably due to sacro-iliac arthritis (Smith-Peterson, 1926). In such patients arthrodesis of the sacro-iliac joint is necessary.

Disruption of the pelvic ring

Fracture or dislocation of the pelvic ring in two places—one posterior in the iliac or sacral portion of the ring, and the other anterior in the pubis—results in gross

instability with marked displacement of one half of the pelvis. The injury may be considered as a hindquarter dislocation or fracture dislocation. As a result of severe torsional violence one half of the pelvis is torn from the other. The common sites of fractures and dislocation are shown in Fig. 110. All combinations of fracture and dislocation may occur.

The fragments are usually widely displaced. The pelvis opens like an oyster shell and the separation of the anterior fragments is maintained by the pull of gravity when the patient is lying on his back (Fig. 111). In addition to the outward rotation the loose fragment of the pelvis frequently rotates in the sagittal plane so that one pubic fragment is displaced above the other (Fig. 112). Finally, the whole hindquarter is often displaced upwards as a result of muscle spasm. Thus the whole hindquarter may be rotated outwards and sagittally and also displaced upwards. Such gross displacement



FIG. 109.—Fracture of the wing of the ilium with displacement of the fragments. The displacement is unimportant.

is easily recognized, for even if the posterior injury is not immediately obvious in the radiographs, the wide separation and displacement of the anterior fragments is certain indication of posterior damage to the ring. Occasionally, the anterior fragments are not greatly displaced, in spite of disruption of one or other sacro-iliac joints In such patients damage to the sacro-iliac joint can usually be detected by careful radiological examination. Recognition of this posterior damage is important, for unless the pelvis is immobilized for a considerable time, persistent back pain will result.

Methods of reduction and immobilization

With disruption of the pelvic ring displacement must be reduced, or there remains persistent back pain which may be very severe. Several methods of reduction and immobilization are described, but of these only two are satisfactory.

The method of lateral recumbency (*Watson-Jones*, 1938).—The patient is held on his side on a plaster table and the displaced half of the pelvis pushed forwards and downwards. When reduction is complete a double hip spica plaster is applied and the patient nursed on his side; the immobilization is continued for three months. This

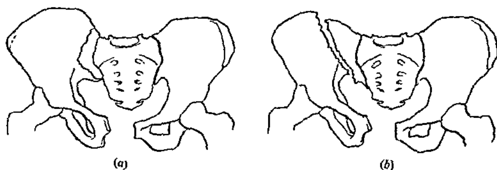
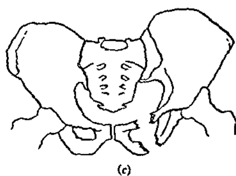


Fig. 110.—Common sites of fracture and dis- [illegible]



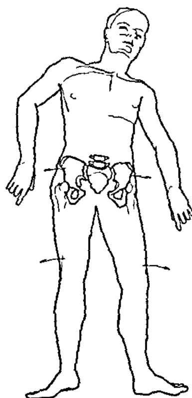


Fig. 111.—With complete separation of half the pelvic ring the fragments open like an oyster shell as a result of the outward roll of the leg (*By courtesy of Messrs. Livingstone.*)



(a)

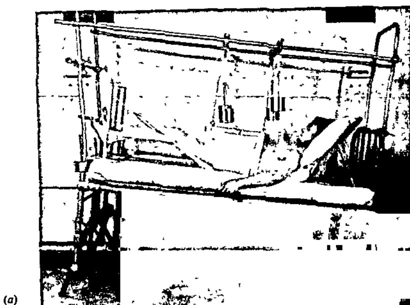


(b)

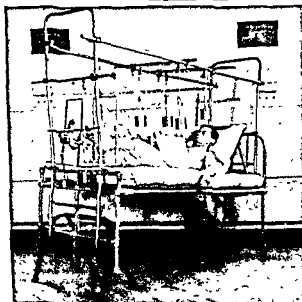
Fig. 112.—(a) Dislocation of the symphysis pubis and right sacro-iliac joint with rotation of the right half of the pelvis. (b) After reduction and immobilization in the pelvic sling.

method is difficult to carry out and unless the plaster is applied with extreme care, large plaster sores may result. Moreover, it is not easy to correct the upward displacement by this method, and even when *reduction is accurate* displacement may recur.

Manipulation and pelvic sling (Fig 113).—The patient is placed upon a bed fitted with an overhead frame. A firm canvas sling spread by rods is placed under the pelvis and



(*a*)



(*b*)

Fig 113 (*a*) and (*b*) —Fracture dislocation of the pelvis Treated in a pelvic sling with weight traction through a Steinmann's pin transfixing the tibial tuberosity. (*By courtesy of Messrs. Livingstone.*)

extended from above the ilium to below the trochanters. The rods are attached by cords to weights which are suspended from pulleys attached to the overhead frame, the cords from the left side passing over pulleys on the right side and *vice versa*. The combined weights are just sufficient to hold the pelvis clear of the bed, and the crossing of the cords produces a *compression force on the separated pelvic fragments*. The legs are supported in flexion on Braun's frames and held there by weight extensions of 8 pounds attached by strapping extensions. It is important that the legs should

be held in flexion at the hip, for if extended the outward roll will reproduce the separation of the fragments.

This simple method will often suffice to reduce and immobilize a fracture or fracture dislocation with pure outward displacement, but if the displaced hindquarter is rotated or displaced upwards, reduction will not be complete.

If rotational deformity is present, this must first be reduced by manipulation under anaesthesia. The manipulation is carried out as described for sacro-iliac subluxation, and when completed the patient is rolled on his back and the sling and frames fixed as described above.

If the fragment is displaced upwards, powerful traction is applied to the affected leg through a Steinmann's pin transfixing the tuberosity of the tibia. This traction is maintained for six weeks and then replaced by strapping extension and a lighter weight.

The degree of compression by the pelvic sling can be adjusted by altering the obliquity of the ropes. Control radiographs are taken and the ropes are adjusted so that the pubic symphysis is kept in position.

Fixation is maintained for twelve weeks, but after six weeks the weights are removed and leg exercises allowed. Weight bearing is allowed after twelve weeks

Nursing in this apparatus is easy. The patient can be lifted by pulling on the weights, and if the lower end of the sling is turned back the bed pan can easily be placed in position. Most patients are comfortable in the sling, though in the very old there may be some mental confusion in the early stages. The method is simple, safe and efficient (Figs. 114–117).

Complications

Hindquarter dislocations and fracture dislocations may be accompanied by severe complications.

Injury to the bladder and urethra.—There may be intraperitoneal or extraperitoneal tears in the bladder-wall, or the urethra may be torn from the bladder-neck. Injuries to the posterior urethra may also occur.

The sling method of treatment for the fracture dislocation is the method least likely to interfere with the after-treatment of these severe complications.

Retroperitoneal bleeding.—Severe retroperitoneal bleeding may occur, and is probably due to the tearing of the ilio-lumbar artery. The loss of blood may be sufficient to cause death, and, indeed, in one series of cases this was the commonest cause of death (Holdsworth, 1948). The patient shows all the signs of internal haemorrhage, and occasionally a haematoma may be observed in the muscle planes tracking towards the anterior superior spine. The bleeding cannot be stopped by pressure, and surgical measures may not be feasible. All that can be done is to maintain the blood pressure at about 100 milligrams of mercury by controlled transfusion.

Sacro-iliac and pubic pain.—The injury may be followed by severe and persistent backache situated over the affected sacro-iliac region. Persistent pain of this type is more common after sacro-iliac dislocation than after fracture near the sacro-iliac joint. The pain persists for as long as two years, but in most cases slowly subsides. A firm supporting pelvic belt gives relief, but if the pain persists sacro-iliac arthrodesis is the best method of treatment.

Many patients complain of aching and tenderness over the pubic fracture. This pain, whilst not incapacitating, can be very troublesome. It is eased by a belt and always disappears in time.



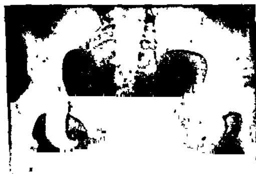


FIG. 114.—Fracture of the pubis and fracture of the ilium with upward displacement of the fragment of the pelvis.





FIG. 115.—The same after reduction and immobilization in the pelvic sling with skeletal traction on the affected leg.



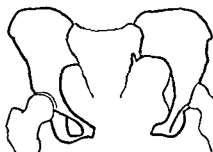


FIG. 116.—Wide dislocation of the symphysis pubis. Dislocation of the sacro-iliac joint.





FIG. 117.—The same patient as in Fig. 116 after reduction and immobilization in the pelvic sling.

(Figs. 114–117 by courtesy of Messrs. Livingstone.)

FRACTURE OF THE SACRUM

Crack fractures of the sacrum without displacement are usually due to direct violence. Occasionally the lower fragment may be displaced, but to no great extent, and is unimportant. A few weeks' rest is all the treatment necessary.

FRACTURE OF THE COCCYX

Fractures of the coccyx with forward displacement are common, and are due to falls *in the sitting position* Pain on pressure on the coccyx whilst sitting, or on defaecation, may persist for months After some weeks the pain which has remained localized to the coccyx may radiate to the buttocks.



Fig. 118.—Fracture of the acetabulum with central dislocation of the hip.

Protection of the coccyx from pressure when sitting is usually sufficient treatment and the pain slowly subsides. Occasionally, however, it persists and may necessitate removal of the c [illegible] with care The whole coccyx must be [illegible] Unless this is done the [illegible]

FRACTURE OF THE ACETABULUM

Fractures of the base of the acetabulum due to falls upon the trochanter produce displacement of the femoral head into the pelvis, for example, central fracture *dislocations of the hip* (Fig. 118).

Treatment

The acetabulum is shattered and accurate replacement of the *fragments is impossible*. The head of the femur can, however, be replaced in its normal position by powerful

traction through a pin transfixing the tuberosity of the tibia with the leg supported in abduction on a Braun's frame. Traction should be combined for 6–8 weeks, followed by graduated non-weight bearing exercises.

Prognosis

The prognosis of these injuries is very bad. In most patients the hip remains painful and limited in movements due to rapid development of a degenerative arthritis. If there is persistent pain in the joint with severe arthritic changes, arthroplasty or arthrodesis should be performed without delay.

(*See also British Surgical Practice:* Fractures, Dislocation, Fracture-Dislocations and Allied Injuries, Vol. 4, page 165, S. Key 157)

BIBLIOGRAPHY

Bohler, L. (1935). *The Treatment of Fractures*, 4th ed Bristol, Wright.
Cooper, Sir Astley (1842) *A Treatise on Fractures and Dislocations of the Joints*, London, Churchill.
Holdsworth, F W (1948) "Dislocation and Fracture-dislocation of the Pelvis," *J Bone Jt Surg.*, 30B, No. 3, 461.
Lewin, P. (1927) "The Coccyx—its Derangements and Treatment," *Surg Gynec Obstet.*, 14, 705.
Smith-Peterson, M N. (1926) "End-results of Sacro-iliac Arthrodesis for Arthritis, Traumatic and Non-traumatic," *J. Bone Jt Surg*, 8, 118.
Watson-Jones, R (1938) "Fractures and Fracture Dislocations of the Pelvis," *Brit J. Surg.*, 25, 773.
— (1943) *Fractures and Joint Injuries*, 3rd ed, p 337. Edinburgh, Livingstone

PORTAL HYPERTENSION

By R. MILNES WALKER, M.S., F.R.C.S.
Professor of Surgery, University of Bristol;
Surgeon, United Bristol Hospitals

INTRODUCTION

The portal circulation concerns the surgeon when changes occur which affect the flow of blood through its vessels, and consequently the patient's health may be impaired and his life threatened. In nearly all cases these changes are the result of obstruction to the normal flow which causes a damming up of blood and increased pressure behind the obstruction; if the obstruction is complete and an outlet is not available for the blood by other channels the blood will be brought to a standstill and thrombosis will occur. An accurate knowledge of the anatomy and physiology of the portal venous system is therefore necessary if the effects of this obstruction are to be appreciated.

ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS

The portal circulation contains venous blood which has passed through the capillaries of the abdominal viscera and it terminates in the sinusoids of the liver where the blood mixes with arterial blood from branches of the hepatic artery. The detailed anatomy of the liver lobules has been closely studied recently; Knisely, Block and Warner (1948) have shown by examination of the blood flow in the margin of the liver of living animals that both portal venous and hepatic arterial blood enter the sinusoids at the periphery of the lobule, and the two become more intimately mixed as the central part of the lobule is approached. In addition there are a few anastomoses between the arterial and venous branches in the portal tracts so that some mixture of blood may occur even before the sinusoids are reached. The extent to which oxygen has been removed from the blood in the abdominal viscera varies from time to time, and during digestive activity much more oxygen is utilized (Smythe and his colleagues, 1951), while it is probable that during resting periods some of the blood actually by-passes the alimentary capillaries through arteriovenous shunts such as those which have been demonstrated in the stomach wall (Barclay and Bentley, 1949). Thus, during health there is undoubtedly a considerable variation in both the composition and the rate of flow of the blood entering the portal circulation. In a like manner there is also a variation in the means by which the portal blood leaves this circulation through the sinusoids of the liver. Seneviratne (1950), working with transilluminated livers of animals, showed that the rate of flow in the sinusoids does not depend on their calibre only, and stimulation of the sympathetic nerves caused contraction of the sinusoids. Daniel and Pritchard (1951) have demonstrated by radiographic methods in animals that in certain circumstances the blood flow through the liver is confined to short wide sinusoids situated centrally in the liver, while on other occasions the blood flow is more evenly distributed through the sinusoids of the whole organ. Presumably, when the short central sinusoids are widely open, less resistance is offered to the flow of portal blood through the liver. The pressure gradient in the portal circulation is not large, but as the flow is from the small venules towards the liver the pressure is lower in the portal vein than in the small venous radicles (Macpherson, 1953). Normally there is little difference in pressure between the portal vein and the inferior vena cava, so that it requires only a slightly increased

resistance to the flow of blood through the liver to raise the pressure in the portal system.

The influence which the hepatic artery blood exerts in maintaining the portal blood pressure is uncertain; in health it probably plays very little part, and observations which I have made at operation in patients with normal livers have failed to show any appreciable change in portal venous pressure when the hepatic artery has been temporarily occluded for a few minutes. If there is disease of the liver causing obstruction to the flow from the sinusoids, the blood entering the sinusoids from the hepatic artery will raise the pressure in them and in time raise the portal venous pressure so that in cases of portal hypertension, due to cirrhosis of the liver, the hepatic artery plays a part in maintaining the abnormally high pressure, and ligation of the hepatic artery will result in a fall in this pressure. Herrick (1907) showed that the influence of the hepatic artery in maintaining the portal pressure is slight, for in dogs there was a rise in portal pressure of only one millimetre of mercury for every 40 millimetres of mercury rise in arterial pressure. By perfusion, Rienhoff (1951) found that in cirrhosis of the liver the hepatic artery flow encounters less resistance than normal.

It is clear, therefore, that the portal circulation may be influenced by changes in the vessels of entry of blood into the circulation, that is the alimentary capillaries, or by changes in the normal means of exit from the circulation—the liver sinusoids—and different conditions at either of these points may alter both the portal blood flow and the pressure in the portal circulation. As the sinusoids in a healthy liver offer very little obstruction to the flow of blood, in normal circumstances an opening-up of the alimentary capillaries or arteriovenous shunts in the walls of the viscera increase the portal blood flow without materially raising the portal blood pressure.

There may be obstruction to the flow in the portal vessels outside the liver—extra-hepatic obstruction—which will lead to a raising of portal pressure in a part or the whole of the portal circulation, depending on the site of the obstruction If there is obstruction due to abnormalities in the parenchyma of the liver, the condition is described as intra-hepatic obstruction and, of course, affects the whole of the portal circulation

The occurrence of extra-hepatic obstruction makes the gross anatomy of the portal circulation of importance to the surgeon. If the portal vein is obstructed the pressure in the whole of the portal circulation is raised and a condition of portal hypertension is brought about. If the obstruction is confined to the splenic vein, as it rarely is, the condition may conveniently be termed "splenic hypertension". In such cases the sites of termination of the left gastric and inferior mesenteric veins are important, for on this will depend the extent of engorgement of veins in the fundus of the stomach and in the rectum respectively. As a result of 50 dissections Doutre and Cabanié (1952) have shown that in only 40 per cent of cases the left gastric vein terminates in the portal vein, in 44 per cent in the splenic vein and in 16 per cent it joins the confluence of the two main veins of the portal system, the splenic and the superior mesenteric. Similarly, in 34 per cent the inferior mesenteric joins the splenic vein, in 54 per cent it joins the superior mesenteric and in 12 per cent it terminates at the confluence of the two.

If there is an obstruction in any part of the circulation the natural reaction is for a collateral circulation to be opened up, generally by means of enlargement of already existing blood vessels; such collateral vessels can become enlarged in an extraordinarily short space of time. In cases of portal venous obstruction they form at all the sites where the systemic and portal circulations link together—in the retroperitoneal tissues, the ligaments of the liver including the falciform ligament, and at the two ends of the abdominal part of the alimentary canal. These collaterals are all beneficial in that they help to relieve the portal congestion, but those in the submucosa

around the cardiac end of the stomach are dangerous in that they may rupture and cause serious, and often fatal, haemorrhage. Butler (1951) has shown that it is a thin-walled sub-epithelial plexus in the mucosa which runs the whole length of the oesophagus which dilates in portal hypertension and from which fatal bleeding may occur; in addition there are submucous veins which run mainly in a longitudinal direction as well as extensive vessels on the outer surface of the oesophagus which constitute no danger to the patient.

In the foetus the umbilical vein terminates in the branch of the portal vein to the left lobe of the liver and may not become completely obliterated after birth, in some cases the hepatic portion remains patent and if such a patient happens to get cirrhosis of the liver this vein, or a branch of it, such as the vein of Burow, will enlarge and become an important collateral between the portal and systemic circulations (Butler, 1952) (Fig. 119). The increased flow in this enlarged vein may cause a thrill and murmur, this combination being known as the Cruveilhier-Baumgarten syndrome (Armstrong and his colleagues, 1942) (Fig. 120).

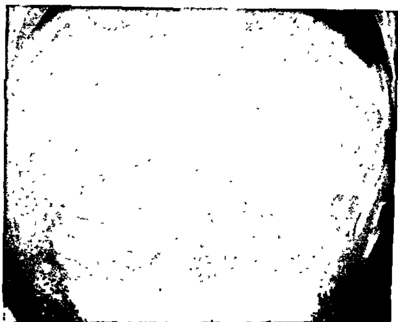


Fig. 119.—Portal venogram by intra-splenic injection in a case of intra-hepatic obstruction. The portal vein is normal; a large umbilical vein is seen coming off its branch to the right lobe of the liver.

PATHOLOGY OF PORTAL OBSTRUCTION

From what has already been written it will be clear that the surgeon's interest is in those cases in which there is obstruction to the normal flow of blood through the portal circulation. This obstruction may be due to disease of the liver—intra-hepatic obstruction—or it may affect the portal blood stream before it reaches the liver—extra-hepatic obstruction.

Intra-hepatic obstruction

Intra-hepatic obstruction is always due to disease in the liver itself. Any disease which tends to obstruct the blood flow through the organ may raise the portal-venous pressure, and we have found raised pressures in cases of extensive metastatic carcinoma; but usually there is fibrosis, though it appears that in some cases of fatty infiltration the cells may become so laden with fat that they compress the sinusoids and obstruct the flow of blood through them. There may be a specific cause of the fibrosis as in cases of haemochromatosis, schistosomiasis or sarcoidosis (Mino.

Murphy and Livingstone, 1949), and a proportion are a sequel of acute infective hepatitis (Dible, McMichael and Sherlock, 1943), all phases between the acute attack and the subsequent fibrosis having been studied by serial liver biopsies (Dible, 1951). In many cases there is no obvious cause, but some give a history of chronic alcoholism, and here liver deficiency rather than the effects of portal venous obstruction dominates the picture. There is no evidence to support the view (Tidy, 1952) that haemor- [illegible] of the new born is a factor of importance in the aetiology and, in fact, the [illegible] ases of cirrhosis [illegible] ous channels in the liver and thus impede the flow of blood through them. The actual quantity of

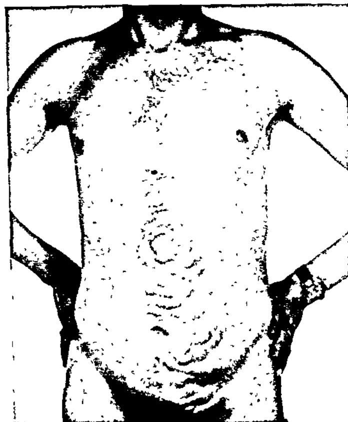


FIG 120—Cruveilhier-Baumgarten syndrome showing very large subcutaneous veins in the subcutaneous tissues of the abdominal wall A thrill and murmur were present just above the umbilicus

fibrous tissue in the liver bears no relation to the degree of portal hypertension, for patients with severely fibrotic livers may have a normal portal venous pressure, while others who have only fine strands of fibrous tissue running through the liver parenchyma have pressures which are three or four times the normal (Walker, 1952). In some cases the fibrous tissue is confined to the portal tracts, thus compressing the branches of the portal vein, but in others fine strands of fibrous tissue spread out from the portal tracts and may link up one portal tract with its neighbours; in the more severe cases, the result of necrosis, all normal liver pattern is lost and areas of parenchyma are isolated from their neighbours by masses of fibrous tissue which incorporate both the portal tracts and the central veins. Clinical evidence suggests that these are not stages of one process, but depend on the damage to the liver by some initial incident—for example, an attack of acute infective hepatitis—and that they do not proceed from one type to the next unless a new episode of active disease affects the liver. In the group where fibrosis is widespread there is, as a rule, clinical

or biochemical evidence of disturbance of the normal liver functions and these changes are likely to be progressive. As regards the other types, little or no change in the liver structure or function may occur over a considerable period of years as shown by serial biopsies and the clinical state of the patient. It is suggested (Walker, 1952) that when the obstruction incorporates the central veins, congestion occurs in the sinusoids and this is an important factor in bringing about progressive hepatic failure. Bolton and Barnard (1931) showed that obstruction of the hepatic veins leads to dilatation of the sinusoids and later to centrilobular necrosis. In cirrhosis there is an increase in the anastomoses between the hepatic artery and portal vein in the portal tracts; if the portal vein is temporarily occluded there is only a slight fall in the pressure in the vein on the hepatic side of the occlusion, in fact in one of my cases there was actually a rise indicating a reversal of flow in the portal vein.

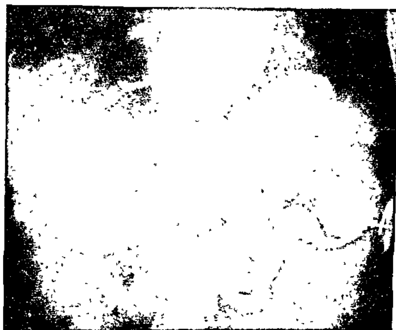


FIG. 121.—Portal venogram by intra-splenic injection in a case of intra-hepatic obstruction. The portal vein is narrowed by secondary thrombosis, and filling defects are present in the splenic vein due to the same cause.

Extra-hepatic obstruction

In cases of extra-hepatic obstruction the liver remains normal histologically. As a rule the obstruction is in the portal vein itself and so involves the whole of the portal circulation; cases which affect the splenic vein alone are rare. Complete occlusion of the superior mesenteric vein results in gangrene of the intestine and is rapidly fatal, so that this form of localized obstruction does not come into the picture. Most cases of extra-hepatic obstruction are due to a congenital abnormality of the portal vein which is represented by a mass of varicose channels ending blindly above, or having inadequate communications with veins in the portal systems of the liver. This condition has been described as "cavernomatous transformation" of the portal vein. In the remainder there is a stricture or atresia of the vein, probably a developmental abnormality. The cavernomatous transformation is also probably developmental in origin, but may be the result of thrombosis at the time of birth and extensive irregular recanalization.

[illegible] in the [illegible]

by a malignant growth. Hunt (1952) described a case due [illegible] nephroma, and Grunberg, Blair and Hill (1952) one due to a pancreatic cystadenoma. In this group the treatment is that of the primary disease.

Patients with intra-hepatic obstruction of long duration are liable to thrombosis of the portal vein and its tributaries, thus adding an extra-hepatic element of obstruction. In three such cases I have exposed the portal vein and found it completely occluded, and in a number of others there has been evidence of an organized mural thrombus. Fig. 121 shows a venogram of a portal vein narrowed by such a cause.

Post-hepatic obstruction

Where there is a rise in pressure or obstruction in the hepatic veins, disturbance of liver function results and the back-pressure is transmitted through the liver sinusoids to the portal system. Sustained increased pressure in the hepatic sinusoids leads to pathological changes in the liver which may add an intra-hepatic to a post-hepatic obstruction which complicates the clinical picture, but this is mentioned in order to avoid mistakes in diagnosis which may otherwise arise. Thus tricuspid incompetence, constrictive pericarditis and the Budd-Chiari syndrome of obstruction to the hepatic veins must be considered as indirect causes of portal hypertension.

MEASUREMENT OF PORTAL VENOUS PRESSURES

There is no satisfactory method of measuring the portal venous pressure in man, and most of the recordings have been taken when the abdomen is open at a laparotomy, but evidence suggests that figures obtained in this way are fairly accurate. The level of the portal vein should be taken as zero. Readings may be made with a water manometer attached to a needle or a canula inserted into a tributary of the portal vein and for this purpose the right gastro-epiploic vein or a vein in the mesentery of the small intestine is the most convenient. A transducer valve or strain-gauge manometer is more useful as accurate readings can then be obtained with the use of a fine-bore needle so that a number of readings in different parts of the portal system can be obtained with the least disturbance of the tissues. It is most important to be sure that there is no pressure on the veins between the part being tested and the liver or else abnormally high readings will be given, in fact the manometer should show some respiratory excursion which demonstrates that the flow is quite free. Allison (1951) has attempted to measure the pressure in oesophageal varices by inserting a needle into them through an oesophagoscope, but this will not give a true reading of the portal venous pressure, for by the time the blood reaches these varices it has flowed some distance from the site of obstruction and must therefore be at a lower pressure than the true portal venous pressure.

NORMAL PORTAL VENOUS PRESSURE

There is normally a slight fall in pressure as blood flows from the smaller venous radicles of the portal system to the main portal vein. Macpherson (1953) found that the differences between a peripheral vein and a larger omental vein may be about 50 millimetres of water, while between an omental vein and a direct tributary of the portal vein it may be even greater. My own cases have not shown such wide variations, but unless recordings are made with a two-channel manometer, which will give simultaneous readings, these results must be accepted with caution. With the patient lying prone I consider that the normal pressure in the portal vein or one of its larger tributaries is between 100 and 150 millimetres of water, taking the level of the portal vein as a basic line. Gray (1951) considers that the upper limit of normal pressure is higher, about 210 millimetres of water. It appears to bear no relation to the systemic arterial pressure, but the influence of drugs which affect the vasomotor tone of the splanchnic vessels has yet to be worked out. Many cases of quite severe fibrosis of the liver have pressures within the normal range.

or biochemical evidence of disturbance of the normal liver functions and these changes are likely to be progressive. As regards the other types, little or no change in the liver structure or function may occur over a considerable period of years as shown by serial biopsies and the clinical state of the patient. It is suggested (Walker, 1952) that when the obstruction incorporates the central veins, congestion occurs in the sinusoids and this is an important factor in bringing about progressive hepatic failure. Bolton and Barnard (1931) showed that obstruction of the hepatic veins leads to dilatation of the sinusoids and later to centrilobular necrosis. In cirrhosis there is an increase in the anastomoses between the hepatic artery and portal vein in the portal tracts; if the portal vein is temporarily occluded there is only a slight fall in the pressure in the vein on the hepatic side of the occlusion, in fact in one of my cases there was actually a rise indicating a reversal of flow in the portal vein.

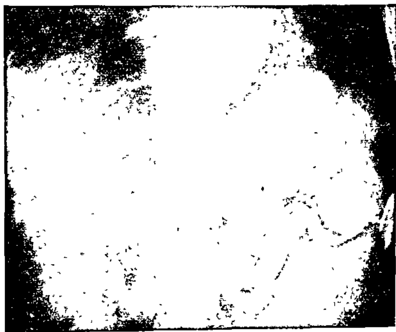


Fig. 121.—Portal venogram by intra-splenic injection in a case of intra-hepatic obstruction The portal vein is narrowed by secondary thrombosis, and filling defects are present in the splenic vein due to the same cause.

Extra-hepatic obstruction

In cases of extra-hepatic obstruction the liver remains normal histologically. As a rule the obstruction is in the portal vein itself and so involves the whole of the portal circulation; cases which affect the splenic vein alone are rare. Complete occlusion of the superior mesenteric vein results in gangrene of the intestine and is rapidly fatal, so that this form of localized obstruction does not come into the picture. Most cases of extra-hepatic obstruction are due to a congenital abnormality of the portal vein which is represented by a mass of varicose channels ending blindly above, or having inadequate communications with veins in the portal systems of the liver. This condition has been described as "cavernomatous transformation" of the portal vein. In the remainder there is a stricture or atresia of the vein, probably a developmental abnormality. The cavernomatous transformation is also probably developmental in origin, but may be the result of thrombosis at the time of birth and extensive irregular recanalization.

Acquired extra-hepatic obstruction is rare; it may be caused by thrombosis in the portal vein in patients with diseases which predispose to spontaneous thrombosis, [illegible] from outside, or its infiltration [illegible] ided hyper- [illegible] ystadenoma.

Patients with intra-hepatic obstruction of long duration are liable to thrombosis of the portal vein and its tributaries, thus adding an extra-hepatic element of obstruction. In three such cases I have exposed the portal vein and found it completely occluded, and in a number of others there has been evidence of an organized mural thrombus. Fig. 121 shows a venogram of a portal vein narrowed by such a cause.

Post-hepatic obstruction

Where there is a rise in pressure or obstruction in the hepatic veins, disturbance of liver function results and the back-pressure is transmitted through the liver sinusoids to the portal system. Sustained increased pressure in the hepatic sinusoids leads to pathological changes in the liver which may add an intra-hepatic to a post-hepatic obstruction which complicates the clinical picture, but this is mentioned in order to avoid mistakes in diagnosis which may otherwise arise. Thus tricuspid incompetence, constrictive pericarditis and the Budd-Chiari syndrome of obstruction to the hepatic veins must be considered as indirect causes of portal hypertension.

MEASUREMENT OF PORTAL VENOUS PRESSURES

There is no satisfactory method of measuring the portal venous pressure in man, and most of the recordings have been taken when the abdomen is open at a laparotomy, but evidence suggests that figures obtained in this way are fairly accurate. The level of the portal vein should be taken as zero. Readings may be made with a water manometer attached to a needle or a canula inserted into a tributary of the portal vein and for this purpose the right gastro-epiploic vein or a vein in the mesentery of the small intestine is the most convenient A transducer valve or strain-gauge manometer is more useful as accurate readings can then be obtained with the use of a fine-bore needle so that a number of readings in different parts of the portal system can be obtained with the least disturbance of the tissues. It is most important to be sure that there is no pressure on the veins between the part being tested and the liver or else abnormally high readings will be given, in fact the manometer should show some respiratory excursion which demonstrates that the flow is quite free. Allison (1951) has attempted to measure the pressure in oesophageal varices by inserting a needle into them through an oesophagoscope, but this will not give a true reading of the portal venous pressure, for by the time the blood reaches these varices it has flowed some distance from the site of obstruction and must therefore be at a lower pressure than the true portal venous pressure.

NORMAL PORTAL VENOUS PRESSURE

There is normally a slight fall in pressure as blood flows from the smaller venous radicles of the portal system to the main portal vein Macpherson (1953) found that the differences between a peripheral vein and a larger omental vein may be about 50 millimetres of water, while between an omental vein and a direct tributary of the portal vein it may be even greater My own cases have not shown such wide variations, but unless recordings are made with a two-channel manometer, which will give simultaneous readings, these results must be accepted with caution With the patient lying prone I consider that the normal pressure in the portal vein or one of its larger tributaries is between 100 and 150 millimetres of water, taking the level of the portal vein as a basic line. Gray (1951) considers that the upper limit of normal pressure is higher, about 210 millimetres of water It appears to bear no relation to the systemic arterial pressure, but the influence of drugs which affect the vasomotor tone of the splanchnic vessels has yet to be worked out. Many cases of quite severe fibrosis of the liver have pressures within the normal range.

Gray and Whitesell (1950) have suggested that in some cases of oesophageal varices in which no portal venous obstruction can be demonstrated the varices may be caused by stasis or congestion in the azygos system of veins. They admit that experimental and clinical proof are lacking, and in my own experience I have never found a case in which some abnormality of the portal system could not be demonstrated. Occasionally patients are found with a normal portal pressure and yet have oesophageal varices; the explanation may be that in the past they have had raised pressures, but that either the cause of the raised pressures—for example, fatty infiltration of the liver—has disappeared or that a collateral circulation has opened up which is adequate to drain away the portal blood and so bring the pressure down to the normal range. It is unlikely that varices, once formed in the oesophagus, will ever disappear completely unless they become occluded by thrombosis, and cases are recorded of haemorrhage from such varices even after a large portal systemic venous anastomosis has been made.

In cases of portal hypertension pressures up to 650 millimetres of water may be recorded. Blakemore (1952) considers that there is rarely danger of severe haemorrhage unless the pressure is above 300 millimetres of water, and in 160 cases he has found only two with pressures below this level, and a history of recent bleeding. My own experience includes nine cases with pressures below this level when bleeding has occurred.

SYMPTOMS OF PORTAL VENOUS OBSTRUCTION

The clinical symptoms of portal venous obstruction depend partly on the collateral circulation which results from the obstruction and partly on the cause of the obstruction. There are many cases in which the cause is the dominating feature and the venous obstruction is only of secondary importance. This applies to the majority of cases of cirrhosis of the liver in which the symptoms are the result of deterioration of liver function and not due to the obstruction of portal venous blood flowing through the liver. There is so far no convincing evidence that surgical measures which are designed to reduce the portal blood pressure have any beneficial influence on the function of the liver, but, of course, in assessing the risk of operating on any of these patients the state of the liver must be taken into consideration.

Symptoms due to the collateral circulation

Bleeding may occur into the alimentary canal at the two sites where the portal [illegible] in the submucous layers. The important site is in [illegible] varicose veins which have already been described [illegible] in the submucous [illegible] may rupture, either as a result of trauma from the passage of irregular food particles or possibly as a result of their erosion by the acid gastric juice (Baronofsky, 1949). In the majority of cases the bleeding comes from the oesophagus, but unless careful inspection is made at necropsy [illegible] patients who die the bleeding point may not be found, as the veins collapse [illegible] of full- [illegible] may precipitate a haemorrhage, but in others the actual onset [illegible] later in the [illegible] occurred. The amount of blood may be slight or may amount [illegible] for a patient to lose his [illegible] promptly [illegible] serious [illegible] life as a r[illegible] attacks. [illegible] than the [illegible] days to [illegible] The interval between successive haemorrhages varies greatly [illegible]

several years, the longest interval in my experience being 13 years, but if there is cirrhosis of the liver, which is progressive, the intervals are likely to be short; according to Patek and his colleagues (1948) 50 per cent of this group die within a year of their first haemorrhage.

Varicosity of the submucous veins of the anal canal also occurs, this being a site of anastomosis between the portal and systemic circulations, and presents as internal haemorrhoids; they are rarely a prominent feature except in older patients, at an age at which internal haemorrhoids are common in any case, so it is difficult to assess the part which the portal hypertension plays in their aetiology. The bleeding from this cause is rarely alarming and calls for no special treatment, but the association with portal hypertension should be realized, for in the presence of such hypertension operative treatment of the haemorrhoids is unlikely to be successful and will be followed by early recurrence

Thus, bleeding from the alimentary canal is the only symptom which is directly due to the portal hypertension In many patients ascites is also present, but this is due to the disease in the liver, for those patients with extra-hepatic venous obstruction never develop ascites from this cause. Thus, the presence of free fluid in the abdomen indicates intra-hepatic disease It is probable that when once ascites has occurred due to disturbance of liver function the raised portal venous pressure may aggravate it, for operations which are designed to lower the portal venous pressure do appear to diminish the accumulation of ascitic fluid in a few cases, but there are other possible explanations for this. There has been much speculation regarding the nature of the ascites in these cases, but Cain and his colleagues (1947) showed that in experimental ascites the flow of lymph from the liver is greatly increased, and Gray (1951) has suggested that this may contribute to the ascitic fluid, certainly sometimes very large distended lymphatics coming from the liver around the portal vein are found at operation When ascites is present very careful appraisal of the liver function is necessary before any major operation, such as a venous shunt, is undertaken.

Symptoms due to disturbed liver function

Other symptoms which are found in these patients are due to the interference with liver function and need hardly be discussed here. Some indication of the prognosis without operation is given by Douglass and Snell (1950) from their experience at the Mayo Clinic. In an analysis of 444 patients with cirrhosis, of 71 who had haemorrhage before their first visit nearly 50 per cent were dead within one year, and four-fifths in less than 7 years One hundred and eighty-four had jaundice and more than 50 per cent of these died within a year and none survived 7 years. Of 212 with ascites, two-thirds died within a year and only 9 per cent were alive after 7 years.

Symptoms due to hypersplenism

The spleen is always enlarged and may lead to hypersplenism; thus many cases have some degree of leucopenia which affects both the neutrophils and the lymphocytes. A few cases have a severe thrombocytopenia and in consequence may complain of haemorrhagic symptoms—bruising, purpuric spots or persistent bleeding after minor injuries. When hypersplenism is severe, removal of the spleen is indicated as part of the surgical treatment and this is the only justification for splenectomy without some other procedure, for splenectomy alone does not materially lower the portal venous pressure.

DIAGNOSIS OF PORTAL HYPERTENSION

The diagnosis of portal hypertension will be suspected in a patient who has haematemesis and is found to have splenomegaly. It may be suspected in other patients

who are found to have either an enlarged spleen or ascites when complaining of other symptoms; in the majority of these patients careful clinical examination will reveal the cause of *splenomegaly or ascites* and portal hypertension as a diagnosis can be excluded. *In others further investigation will* be necessary.

Clinical examination should be directed particularly to any evidence of liver disease; careful palpation of this organ is necessary, and signs of liver dysfunction—such as brown discoloration of the skin, palmar erythema or spider naevi—looked for. The spleen is rarely grossly enlarged in this condition, but is usually firm and may reach to the level of the umbilicus; its size does not give an accurate estimation of the degree of raised portal pressure.

The next stage in the investigation is a search for varices in the lower end of the oesophagus, for their presence is conclusive evidence that portal hypertension exists, or has recently existed; such varices do not disappear rapidly if the portal pressure returns to normal. The absence of oesophageal varices, however, may be taken as evidence that no serious degree of portal hypertension is present. The easiest way to demonstrate these varices is by a barium swallow, when they show as filling defects disturbing the normal pattern of the longitudinal folds of the mucous membrane of the oesophagus. Sometimes they fail to show by this investigation and in such cases, if the diagnosis is still suspected, resort must be had to oesophagoscopy. At this examination the veins stand out as blue projections into the lumen; in mild cases as isolated swellings, in severe cases as large purple swellings all round the lumen looking very like severe internal haemorrhoids. In long-standing cases the overlying mucous membrane becomes thickened and has a milky-white colour.

There are other investigations which should be carried out before a major operation is decided upon. A blood count is necessary to show the degree of anaemia or any effects of hypersplenism. Liver function tests should always be carried out. Those performed as a routine are. (1) estimation of serum proteins and the relative amounts of albumin and globulin; (2) the serum alkaline phosphatase and flocculation tests such as thymol turbidity and flocculation, and (3) the colloidal gold test. In Great Britain the estimation of the rate of excretion of Bromsulphalein is not often carried out as a routine, but it may be of particular value in cases of portal hypertension and is much used in the United States of America.

The serum albumin estimation is of great value in giving an idea of the amount of functioning liver tissue. If the level is below 3 grammes per cent, and particularly if this is lower than the globulin content, there is anxiety about the state of function of the liver, and a major operation such as a venous anastomosis should be carried out only after preliminary treatment and when the risk of death from haemorrhage is considerable; treatment with a high protein diet may improve the state of affairs and render the risk of operation less serious. In my opinion a serum albumin level which is persistently below 2·5 grammes per cent is a definite contra-indication to any major operation designed to relieve portal hypertension.

The serum alkaline phosphatase is likely to be raised, particularly in cases of obstructive jaundice, and when it is much elevated it usually indicates that, in cases of cirrhosis of the liver, there is some degree of intra-hepatic obstruction of the bile ducts; it is rarely found to be grossly raised in the type of patient who presents with symptoms of portal hypertension, and if it is raised in such cases other liver function tests will also show gross abnormalities.

The flocculation tests are of value, for if they are grossly abnormal there is a *suggestion* that there is active hepatitis and the condition of the liver will be progressive; when this happens it is advisable to wait and try to obtain some idea of the rate of progress of the disease. Some cases have active disease which progresses very rapidly so that the patient will succumb from liver failure and it is obviously unwise to operate. Others may in time show improvement as regards these tests when the active

hepatitis subsides, and if symptoms of hypertension persist then will be the time to consider operation. If, during the active phase of hepatitis, the patient is having serious haemorrhage from oesophageal varices the surgeon will have to consider very carefully whether the risk of a major operation is justified. One of the dangers of delay is that thrombosis may occur in the portal vein or its tributaries and so make the formation of a portal systemic shunt impossible. It is in these doubtful cases that the Bromsulphalein test can be very valuable. Blakemore (1952) puts much reliance on this test and found a mortality of 27·7 per cent if the retention after 30 minutes was over 20 per cent, compared with a mortality of 12 3 per cent with a retention level below this figure.

Peritoneoscopy is an investigation occasionally required, as it will give accurate information regarding the size, consistency and surface of the liver. Puncture biopsy of the liver is of interest in following the progress of the hepatic disease, but does not often give information which influences the treatment of the patient.

PORTAL VENOGRAPHY

It has been my practice during the last year to carry out this most useful investigation on all patients with portal hypertension on whom a portal-systemic shunt is contemplated. The technique has been described (Walker, Middlemiss and Nanson, 1953) and consists in the injection of 30 millilitres of 70 per cent iodine contrast medium into the spleen by a needle inserted through the parietes. The injection is made as rapidly as possible and the first x-ray exposure made as the injection is completed. The contrast medium enters the portal circulation very rapidly and shows the anatomy of the splenic, portal and left gastric veins and of varices around the cardia. In cases of intra-hepatic obstruction some of the medium passes through the liver, but most of it goes by the left gastric vein to the varices (Fig. 121) though some may be seen entering intercostal vessels through the anastomosis in the spleno-renal ligament, and in a few cases a shadow of the inferior mesenteric vein may appear as some of the medium passes down towards the anastomosis in the anal canal. Mural thrombi in the portal vein may show as filling defects or may narrow the whole vein. This investigation will therefore demonstrate before operation if there is a portal vein suitable for a porta-caval anastomosis.

If the obstruction is extra-hepatic the anatomy of the portal and splenic veins will show the type and site of obstruction and thus help in the planning of the operation necessary for its relief (Figs. 122 and 123).

The investigation seems to be safe, but should be attempted only if the spleen is sufficiently enlarged to be palpable; we have seen no untoward effects in the cases in which it has been employed.

SURGICAL TREATMENT OF PORTAL HYPERTENSION

Selection of cases

The selection of cases of portal hypertension which are likely to benefit by surgical treatment calls for considerable thought and will not necessarily be judged the same for all surgeons There is general agreement that a wide venous shunt between the portal and systemic circulations is the best safeguard against dangerous haemorrhage from oesophageal varices. The performance of such a shunt is, however, an operation requiring great care and patience and should never be attempted by a surgeon who is not well versed in the technique of vascular suturing; when dealing with large blood vessels some accidental occurrence may lead to disaster at the time of operation, while a minor error in technique may cause thrombosis at the site of anastomosis and so render the operation quite useless.

The relief of ascites which may be expected as a result of surgical treatment in hepatic cirrhosis is still a matter for conjecture. Blakemore (1952) believes, on his wide experience, that a portal systemic shunt has a place in the treatment of ascites due to this cause, but Linton (1951) holds the contrary opinion. In hepatic cirrhosis



FIG. 122.—Portal ve gram by intra-spl injection in a cas extra-hepatic obst tion, showing comp obstruction of splenic vein. Note large varices ar the cardia.



FIG 123.—Portal venogram, from the same case as in Fig 122, by injection of a tributary of the superior mesenteric vein. The portal vein is replaced by a number of varicose channels.

... coming and going spontaneously ... experience the ... tic treatment, who have ascites which pe... r operation s have such a severe disturbance of liver function that ... portal-systemic shunt is contra-indicated.

Thus the operative measures adopted in the treatment of portal hyperten into three groups: (1) portal-systemic venous shunts; (2) operations on th

themselves, or designed to divert portal blood from the varices, but which do nothing to reduce the portal blood pressure; and (3) ligature of the hepatic artery.

In the present state of our knowledge it appears that the first measure gives the best results if the shunt is wide and remains patent. The measures in the second group can, at the best, be considered only as palliative. The third group may still be regarded as in the experimental stage.

Portal-systemic shunts

To make an effective shunt of blood between the portal and systemic circulations the opening must be a large one, and therefore only large veins are satisfactory for the purpose; also the shunt must be into a large low-pressure vein of the systemic circulation. In effect, therefore, there are only two suitable sites—the portal vein to the inferior vena cava and the splenic vein to the left renal vein. Other sites have been employed, for example, the superior mesenteric vein to the inferior vena cava (Blakemore and Fitzpatrick, 1951), but the results when other smaller veins are used are relatively disappointing and the openings are liable to become occluded by thrombosis.

My own preference is an end-to-side anastomosis between the portal vein and the inferior vena cava.

The portal vein is large and in the case of intra-hepatic obstruction this anastomosis is as near the site of obstruction as possible.

The operation, as carried out through a thoraco-abdominal incision, is not so difficult as a spleno-renal anastomosis.

In performing a spleno-renal anastomosis it is nearly always necessary to remove the spleen as part of the operation, and when this organ is already surrounded by extensive vascular adhesions this alone may be sufficiently formidable without the addition of performing the anastomosis

An end-to-side porta-caval anastomosis has the advantage that the portal vein is less distorted than it is when a side-to-side anastomosis is made.

After an anastomosis the blood in the intra-hepatic portal venous system is stagnant and thrombosis tends to occur In the case of a side-to-side anastomosis there is the theoretical danger of this thrombosis spreading down to, and perhaps occluding, the anastomosis. If the portal vein has been divided and an end-to-side anastomosis performed, this is no longer in direct vascular continuity with the stagnant blood in the veins of the portal tracts

The experimental work which demonstrates that in dogs with normal livers the diversion of all venous blood greatly reduces the capacity for regeneration of the liver, does not appear to apply in those patients in whom much of the venous blood has already been diverted

A healthy portal vein is not available for making an anastomosis in the majority of patients with extra-hepatic portal obstruction and in a proportion of cases of intra-hepatic obstruction who have developed secondary thrombosis of the portal vein. Portal venography is most valuable in detecting this group, and in them a spleno-renal anastomosis is the next alternative. This is usually performed by joining the end of the splenic vein to the side of the left renal vein, after removal of the spleen. I have performed a few cases of side-to-side spleno-renal anastomosis in patients in whom the splenic vein is large and tortuous and can easily be brought to lie in contact with the left renal vein, so avoiding the additional risk to the patient of removing a large spleen with many vascular adhesions. Even if the spleen is not removed the splenic artery should be divided between ligatures. In a few cases the splenic vein also is obliterated by thrombosis and in this difficult group no satisfactory anastomosis can be made. Into this group also fall those cases of extra-hepatic obstruction who have already been subjected to splenectomy.

Pre-operative preparation

Before any of these vascular shunt operations are carried out certain pr
are necessary. At least two litres of blood for transfusion must be avail
danger is not from the large vessels but from oozing from the numerous c
channels which are encountered around the portal vein in a porta-caval sh
in the ligaments of, or adventitious adhesions to, the spleen in a spleno-ren
tomosis. Both these operations are most easily performed through thoraco-ab
incisions (the former on the right and the latter on the left) so that in eit
physiotherapy to aid expansion of the chest is most valuable.

Porta-caval anastomosis

The patient is placed on the operating table turned towards his left side
the anterior axillary line is uppermost. The incision follows the line of the ni
from the posterior axillary line forwards to a point about five centimetres bey
costal margin; the length of the ninth rib so exposed is removed and the corr
ing costal cartilage split longitudinally, a step which simplifies the reconstit
the costal margin during the closure. The abdomen is opened at the front
incision carried back along the rib bed to open the pleura. From the point of
ment of the diaphragm thus exposed the latter is incised radially as far as the c
ligament of the liver; this allows the liver to be retracted upwards, giving g
posure of the lower surface of its right lobe, unless it is enlarged and unduly
factor which may make the exposure of the portal vein much more difficult. I
of the peritoneal reflexion between the right kidney and the liver will usuall
further displacement of the latter upwards. There are often many small vessels
fold, some of which may require ligatures. Oozing from the liver itself, if the f
been cut too close to the liver, is best stopped by the coagulating diathermy c
The foramen of Winslow is now located, bearing in mind that it may be obli
by adhesions. A V-shaped incision is made in the peritoneum of the anterior,
and posterior margins of the foramen and is continuous with the previous i
posteriorly over the vena cava. Usually many small blood vessels lie in the con
tissue so exposed behind the common bile duct, but enlarged lymphatic chann
sometimes lymph nodes are found here and access may be improved by rem
one or more lymph nodes. Patient dissection with gauze pledglets eventually e
the portal vein which is thicker-walled than most veins, and when once expos
usually be freed, without great difficulty, from the surrounding connective tis
the vein is adherent it always indicates that there has been thrombosis inside
the lumen may not be completely obliterated and we have used a number of vei
porta-caval anastomosis in which an organized mural thrombus has been p
It is necessary to [illegible] the vein, and if possible th
main branches int [illegible] the liver should be expose
ligated separately [illegible] at there is no possibility of
ligatures slipping.

Attention is next paid to the inferior vena cava, and its anterior surface is cl
[illegible] or 5 centimetres. Its close attachment to the
[illegible], often necessary to expose it below as far a
[illegible] t be cleared to allow 2·5 centimetres to be pi
up in a clamp [illegible] ge everything is ready for ligature and divisi
the portal vein and performance of the anastomosis, but in order to place the su
correctly, good access and good illumination are essential. A Blalock clamp is pl
on the portal vein as low down as possible, the ligatures on the upper end c
branches tied and the vein cut across 0·5 centimetre below the ligatures. This al
the vein to be rotated from behind the common bile duct and makes it more acces
for the anastomosis. A light curved clamp such as that devised by Satinsky (I

now picks up the anterior wall of the inferior vena cava and an incision made into it as long as the width of the portal vein (Fig. 124*b*); the anastomosis is made using fine silk everting continuous mattress sutures as for any vascular suture (Fig. 124*c*). When the clamps are removed one or two extra stitches may be required, and often the blood may be seen eddying in the inferior vena cava through its thin wall. The anastomosis being complete, a slice of liver is taken for biopsy, the diaphragm sutured and the wound closed, leaving a tube down to the pouch of Rutherford-Morison, brought out through the anterior end of the wound and connected to an underwater seal. No heparin is given.

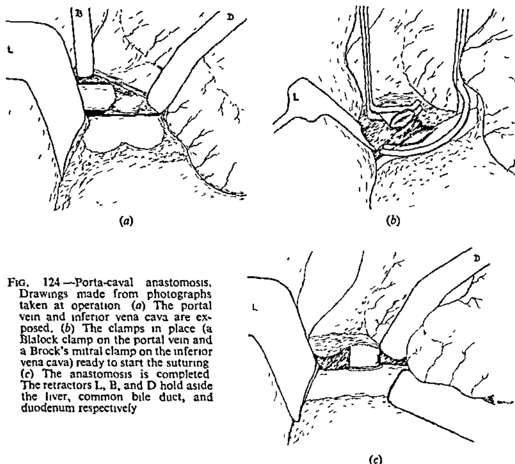


Fig. 124.—Porta-caval anastomosis. Drawings made from photographs taken at operation (*a*) The portal vein and inferior vena cava are exposed. (*b*) The clamps in place (a Blalock clamp on the portal vein and a Brock's mitral clamp on the inferior vena cava) ready to start the suturing (*c*) The anastomosis is completed The retractors L, B, and D hold aside the liver, common bile duct, and duodenum respectively

Theron (1953) has advocated the use of a vein graft in preference to a direct porta-caval anastomosis, claiming that less mobilization of the portal vein is necessary and a wider communication can be made. I have used a graft only once, in a patient whose portal vein could not be approximated to the inferior vena cava.

The patency of a porta-caval shunt can be demonstrated by portal venography. Fig. 125*a* shows that no blood is entering the collaterals, but is passing through the anastomosis into the inferior vena cava, while Fig. 125*b* demonstrates the increased rate of flow.

Spleno-renal anastomosis

This operation is carried out most satisfactorily by a thoraco-abdominal approach on the left side with resection of the ninth or tenth rib. The great omentum is divided along the greater curvature of the stomach at an early stage so that the splenic artery

can be ligated before the spleen itself is mobilized and before its ligaments and any adhesions, which are usually very vascular, are divided. Splenectomy is then carried out, dissecting the individual vessels in the hilum and preserving as much of the splenic vein as possible. A bulldog clamp is placed on the proximal end of the vein



FIG. 125.—Portal venogram after an end-to-side porta-caval anastomosis (same case as shown in Fig 119). (a) The opaque solution passes through the anastomosis and none enters the left gastric vein or the varices (b) Four seconds after completion of injection.

(a)



(b)

before it is divided and any blood washed out with saline. By dissection in the retroperitoneal tissues the renal vein is exposed and at least 2 5 centimetres of its length isolated, any tributaries which enter this portion of the vein being ligated. If the swelling of the kidney which occurs when the renal vein is clamped is such that it impairs access to the renal vein, it is wise to isolate the artery also and place a bulldog clamp on this. No damage to renal function has been observed when these clamps have been left on for periods up to twenty minutes, but they are not put in position

until everything is ready for making the anastomosis. It is important that the two veins should come into apposition without tension and for this it may be necessary to mobilize the tail of the pancreas with the splenic vein, care being taken of the small tributaries which enter the latter from the pancreas. Two Blalock clamps may be placed on the renal vein, but a more satisfactory plan is to place a Blalock clamp on the proximal end and two temporary ligatures on the two main tributaries of the renal vein in the hilum of the kidney—they take up less room than a clamp and gentle traction on them keeps the vein taut To make the anastomosis a transverse incision is made in the renal vein and its margins are sutured to the splenic vein with everting continuous mattress sutures. For such an anastomosis to be worth while the splenic vein should be at least one centimetre in diameter, as if a vein smaller than this is used the risk of thrombosis is considerable. In portal hypertension it is usual to find a wide splenic vein, but in a few cases its lumen is quite small, possibly as the result of previous thrombosis, and if such a vein is used for an anastomosis the result is likely to be disappointing. If there is difficulty in mobilizing the splenic vein, a free vein graft may be employed (Rousselot, 1952). The incision is closed in the same way as in a porta-caval operation, with a temporary drain down to the retroperitoneal tissues.

Post-operative treatment

After operation the complications which may arise are liver failure, thrombosis at the site of anastomosis or thrombosis in other veins, particularly after a splenectomy has been performed. Liberal administration of fluids and glucose are the best means of ensuring adequate liver function. In two cases in our series which went into hepatic coma after such operations, drowsiness gradually deepening into coma first made its appearance about 24 hours after operation. There is some evidence (Walshe, 1953) that glutamic acid is beneficial, and as soon as there is any sign of drowsiness 20 grammes of glutamic acid should be given slowly intravenously in a litre of saline.

Thrombosis of the anastomosis is unlikely to occur, provided the opening is large enough, but Blakemore (1952) has recommended the insertion of a polythene tube into a tributary of the portal circulation near the anastomosis and the instillation of heparin. It is not usual to give anticoagulant drugs as a routine in these cases, but if there is evidence of thrombosis occurring either in the abdomen or in the limbs a short course of heparin should be given.

Operations on the oesophageal varices

The simplest procedure is injection of the oesophageal varices with a sclerosing solution through an oesophagoscope; this was first advocated by Crafoord and Frenckner (1939) but the results are, on the whole, disappointing and it is rarely practised. Ligation of the main veins outside the stomach, particularly the left gastric vein, has been given a trial, but little benefit has accrued and something more radical is necessary. Tanner (1950) suggested not only dividing these vessels, but also cutting the stomach across and resuturing it, thus disconnecting this link between the portal and the azygos systems of veins and leaving a line of scar tissue between them. A similar operation with division of the lower end of the oesophagus—oesophageal transection—has also been employed (Walker, 1952) through a left transthoracic approach, but there is a slight risk of stricture after healing, as well as the theoretical possibility that further bleeding may come from varices in the cardiac end of the stomach. Gastric transection—with division of veins in the lesser omentum and of the vasa brevia, but carried out through the left pleural cavity and an incision in the diaphragm—gives better access than an abdominal approach and is likely to be more effective. The writer has carried out either oesophageal or gastric transection without any operative mortality on 16 patients in whom a venous shunt was impractical.

Oesophago-gastrectomy, with anastomosis of the oesophagus to the stomа thorax, is a more radical procedure; excision of the varix-bearing area advocated by Phemister and Humphreys (1947), and has recently been pra Learmonth (Macpherson, 1953) who claims that the subsequent disturb digestion are not so severe as when a similar operation is carried out for ca Too few cases have so far been reported to assess its value.

Other operations with the same object in view follow similar lines witl modifications. Allison (1950) has advocated extensive ligation of the veins and leaving the oesophagus. Boerema (1949) opens the oesophagus longi and ligates the submucous veins, with injection of sclerosing solution bet ligatures, and Linton and Warren (1953) have recently advocated a similar p in cases of persistent bleeding. Suture of the submucous varices can be combi oesophageal transection, a plan that I have adopted in a few cases. Garlock (1950) have practised packing of the mediastinum around the oesophagus idea of promoting vascular adhesions which will allow freer flow of blood oesophagus into the azygos system. This idea is in line with a suggestion Gray and Whitesell (1950) that the anatomy of the azygos system of veins n factor in some cases of portal hypertension.

The great variety of these operations on the varices is an indication that them are really satisfactory in preventing further haemorrhage.

Ligature of the hepatic artery

This operation is based on experimental work which suggests that in cirr the liver the arterial pressure is communicated to the portal vein branches directly through the increased anastomosis between these vessels or indire raising the tension in the liver lobules. The variation in the anatomy, particul site of origin of the gastro-duodenal artery, leads to some confusion; in son where the ligature is proximal to this branch a good deal of arterial blood still the liver through this anastomosis, and Grindlay (1951) points out that the op is unlikely to deprive the liver entirely of arterial blood. Rienhoff (1951) was to describe this operation, reporting two cases—one complaining of haemat the other of ascites—in whom improvement had lasted 1 year and 3½ years tively at the time of the report.

Berman, Koenig and Muller (1951) recommend the operation on the exp of ten patients who had favourable results, but Madden (1952) had three imn deaths among seven patients and doubts whether the results warrant its cor use. Leger and his colleagues (1952) have tied the hepatic artery in five case two post-operative deaths. McFadzean and Cook (1953) quite independently to the conclusion on the experimental evidence that this operation might be [illegible]

tense ascites. In two it was performed during the course of repeated massive [illegible] There were three post-operative deaths from massive necrosis of the liver an note a word of caution regarding this danger.

Hunt (1952) ligated the hepatic artery in two cases with fatal results, but two in whom he tied the coeliac axis survived, though one was not improved. Rosen and Egbert (1952) reported a patient who died on the second post-operative day ligature of the hepatic artery proximal to the gastro-duodenal branch.

Further reports of this operation are necessary before it can be accepted regular means of treatment; on theoretical grounds it seems wrong to depri already diseased organ of its arterial blood supply. The danger of liver necro evidently serious. It is clearly not indicated in cases of extra-hepatic obstructio should not be performed unless the patency of the portal vein can be demonst

Of the remaining operative procedures which have been given a trial little need be said. Splenic artery ligation alone has been suggested by McNee (1931) and advocated by Blain and Blain (1950), but the results of the operation are unsatisfactory and more than 50 per cent of a small series of personal cases have had further haemorrhage. In the same way splenectomy alone gives disappointing results; in my series all 8 cases of extra-hepatic obstruction in which splenectomy alone was carried out have [illegible]

RESULTS OF PORTAL SYSTEMIC SHUNTS

It has already been pointed out that if a shunt is to be effective it must be a wide one, and the nearer it is to the site of obstruction the better will be the result. If such a shunt remains patent there is small danger of further haemorrhages, though one of my own cases, who had defective liver function, died of haemorrhage seven months after a large porta-caval shunt, and at the necropsy the shunt was quite patent. Linton (1951) has had a similar experience, but Blakemore (1952) states that in not one of his cases in which the shunt remained fully patent has fatal haemorrhage occurred.

There seems to be no evidence that deflection of the portal venous blood in cases of intra-hepatic venous obstruction, as in an end-to-side porta-caval anastomosis, has a detrimental effect on the function of the liver and its regeneration, such as occurs in animals with normal livers when an Eck's fistula is made (Large, Johnston and Preshaw, 1952). Some patients with congenital extra-hepatic biliary obstruction have most or all of their portal blood diverted into other channels, yet they show no evidence of deficient liver function.

Blakemore (1952) has had the largest experience of these operations, now covering 166 operations in 160 patients; his overall mortality has been 18 per cent, but there were only 9 deaths in the last 107 cases, a mortality of 8 4 per cent. Many of his cases had severe liver damage, but in spite of this two-thirds of these were alive two years following operation. He states (Blakemore, 1951) that after a successful shunt the varices disappear or become smaller and that the spleen shrinks and is usually no longer palpable 1½ years after operation. After a porta-caval shunt if the platelets have been reduced in number, they increase but rarely reach a low normal level; similarly the leucocytes increase but not so rapidly as after a splenectomy. He suggests that if there is much evidence of hypersplenism it may be better to perform a splenectomy and spleno-renal shunt rather than a porta-caval shunt. In 18 cases he quotes measurements of portal venous pressure before and after a shunt—before the shunt the maximum figure was 620 millimetres of water and the minimum 255 millimetres, while after the shunt was open the maximum recorded was 290 millimetres of water and the lowest 120 millimetres. Liver function tests have not been materially improved by the operation, but Blakemore (1952) considers that the operation has a place in the treatment of ascites and recommends it if the ascites is persistent and the liver function is not too greatly impaired.

Linton (1951) has reported his experiences in 61 cases in which shunts have been made. He considers that haemorrhage is the only indication, and that it should not be performed as a measure to relieve ascites.

My own experience covers 42 shunts in 40 patients. During the last 3 years, when it has been realized that to be effective a shunt must be large, and if suitable large vessels are not available no shunt is performed, the results have been most encouraging. Except in a few early cases the operation has only been performed to prevent haemorrhage, and cases with severe liver damage have been advised against it. The operative

mortality has been 5 cases, but only 2 have died among the last 30 cases and both these had severe liver damage and are referred to in greater detail below.

The types of anastomosis which have been made are as follows:

	Intra-hepatic obstruction	*Extra-hepatic obstruction*
End-to-side porta-caval	22	—
Side-to-side porta-caval	2	1
End-to-side spleno-renal	9	3
Side-to-side spleno-renal	1	2
Other vessels	1	1

Two patients have had a second shunt; the first was a man aged 31 years with somewhat defective liver function on whom a side-to-side spleno-renal shunt was performed in 1949. He had further bleeding and an oesophageal transection was carried out in 1951, but in spite of this bleeding recurred, so an end-to-side porta-caval anastomosis was made. He had no further trouble for 7 months and then died of uncontrollable haemorrhage from his oesophageal varices; at the necropsy the original spleno-renal shunt was occluded, but the porta-caval shunt was widely patent and the lining free from any thrombus. It is probable that his poor liver function contributed to the failure of the terminal haemorrhage to stop, but this is the only case in the series in which a patient, thought or known to have a widely patent shunt has had further serious bleeding.

The second patient who has had more than one shunt was a boy aged 14 years with extra-hepatic obstruction; at the first operation the lowest tributary of the splenic vein from the spleen was divided and its proximal end anastomosed to the side of the renal vein; the splenic artery was divided but the spleen was not removed. He had no further haemorrhage for 4 years but then had a recurrence; a splenectomy and end-to-side spleno-renal anastomosis was carried out. The previous anastomosis was occluded and the spleen showed areas of old infarction.

There were 3 deaths in the early part of this series, 2 from leakage from the anastomosis and one from mesenteric thrombosis 3 weeks after operation. As already mentioned, 2 further hospital deaths from hepatic coma have occurred. The first was a woman aged 38 years who had severe haemorrhages and somewhat defective liver function. She recovered consciousness fully after the operation, but the next day relapsed into coma; in order to maintain a clear airway tracheotomy was performed, but though she lived for 5 weeks in varying degrees of coma she subsequently died. Intravenous glutamic acid was given a trial and this did appear to have a temporary beneficial effect on the coma. The second patient who died was a man aged 31 years who had had haemorrhages for 8 years and had received a total of more than 50 pints of blood by transfusion; he also had severe [illegible] His liver function [illegible] tient did recover fully from his coma and 4 days later was getting up and seemed to be making normal progress; on the eighth post-operative day, in a bout of coughing, the thoracic portion of his wound gave way, causing an open pneumothorax, and following an operation to repair this he rapidly relapsed into coma which, this time, in spite of the administration of glutamic acid, proved fatal.

The prospects of performing a satisfactory shunt in cases of extra-hepatic

obstruction are not so good, a suitable vein being less frequently available. Thus, in only 4 cases of extra-hepatic obstruction in my series has it been possible to perform a spleno-renal anastomosis. In two of the remainder the splenic vein was very small or thrombosed and in 5 cases the spleen had already been removed.

Short series of porta-caval shunts have been reported by many writers. Pattison (1949), in 10 cases of porta-caval anastomosis, had 2 post-operative deaths, and of 3 of the series in which the operation was performed for haemorrhage there was no recurrence, but 3 of the 5 in whom ascites was the main symptom showed little or no improvement.

Learmonth (1951) reported 19 cases with 5 deaths; 13 had end-to-end spleno-renal anastomoses with removal of both the spleen and kidney, 5 had end-to-side spleno-renal anastomoses and one had a porta-caval anastomosis; 5 cases have had recurrence of symptoms. Stock (1952) performed 11 porta-caval anastomoses, mainly on patients with ascites, with 4 deaths. In a further 4 cases the portal vein was found to be thrombosed, and in the type of patient found in Hong Kong he advocates splenectomy as a preliminary to a porta-caval anastomosis, thrombosis of the splenic vein is so common that he does not advocate spleno-renal anastomosis.

Large, Johnston and Preshaw (1952) had 2 post-operative deaths from hepatic failure in 18 cases, and had 9 very good results among the 12 cases in which haemorrhage was the only symptom.

To sum up, it appears that these operations to shunt blood from the portal back into the systemic vessels can be carried out with a reasonably low risk; they give the patient a good prospect of permanent relief from haemorrhage, but do not influence the pathological condition in the liver. As hepatic failure is the most common cause of post-operative deaths the mortality will depend largely on the selection of cases, and the surgeon has to weigh up the risks of operation against the risks of further haemorrhage in all those patients who show evidence of deficient liver function. That the operation is really of value for the relief of ascites is not yet proved, and as ascites in cases of cirrhosis is always a sign of defective liver function the operation carries a much greater risk when this symptom is present.

EMERGENCY TREATMENT OF HAEMATEMESIS FROM OESOPHAGEAL VARICES

If untreated many of these patients will die of haemorrhage, and emergency treatment plays an important part in getting them over such a crisis. As haemorrhage from this cause accounts for less than 10 per cent of all cases of severe haematemesis, the diagnosis of peptic ulceration is likely to be made. Most of these patients, however, have an enlarged spleen and this should arouse suspicion that varices are the cause of [illegible] eet elevated [illegible] of the cases [illegible] The use of an inflated balloon, either in the oesophagus to compress the varices, or in the stomach with traction made on it to draw it against the cardia and then compress the veins at this point, may be a life-saving measure (Rowntree and his colleagues, 1947). Special balloons have been devised for this purpose, but in an emergency a Miller-Abbot tube will serve. When bleeding persists, in spite of the use of the balloon, direct exposure of the bleeding area through a left thoracic incision has been employed by Boerema (1949) and by Lint[illegible] measure; the bleeding vessels are under-run [illegible] been opened lengthwise; this severe operatio[illegible] bleeding persists in spite of milder measures. Linton advises that it should be followed

by a portal systemic venous anastomosis as soon as the patient has sufficiently recovered from the oesophagotomy.

SUMMARY OF SURGICAL TREATMENT

A portal systemic venous anastomosis is the most effective way of reducing the portal blood pressure in portal hypertension. These shunts are indicated in patients who have had haemorrhage from oesophageal varices which is dangerous to life, or who have very large varices which are likely to bleed. Such operations should not be undertaken if the liver function is severely impaired. The risk is dependent almost entirely *on the state of the liver, but older patients do not tolerate it so well, and in* only the exceptional case can it be justified over the age of 60 years. The nearer the anastomosis is to the obstruction the more effective it is likely to be. At present the clinical evidence is not sufficient to indicate any difference in the results if the portal blood is excluded entirely from the liver, as in an end-to-side anastomosis, or if the portal vein is retained in continuity.

Many alternative procedures have been tried to prevent haemorrhage from oesophageal varices. Methods at present employed include:

(1) Exposure and submucous ligature of the varices after opening the oesophagus.

(2) Gastric or oesophageal transection to cut off the vessels carrying portal blood to the varices.

(3) Excision of the lower oesophagus and upper stomach to remove the main varix-bearing area.

None of these methods are really satisfactory, but they are worth further trial.

Ligature of the hepatic artery has been employed recently. It is contra-indicated in cases of extra-hepatic obstruction, and in those cases of intra-hepatic obstruction with thrombosis of the portal vein. It is technically easier than a venous anastomosis, but carries an appreciable risk of hepatic necrosis.

(*See also British Surgical Practice:* Liver—Cirrhosis, Vol. 5, page 437, S Key 223.)

REFERENCES

Allison, P. R. (1950) *Ann. Surg.*, 132, 808.
— (1951) *Thorax*, 6, 325.
Armstrong, E. L., Adams, W. L., Tragerman, L. J., and Townsend, E. W. (1942). *Ann. intern. Med.*, 16, 113.
Barclay, A. E , and Bentley, F. H. (1949). *Brit. J. Radiol.*, 22, 62.
Baronofsky, I. D. (1949) *Surgery*, 25, 135.
Berman, J. K., Koenig, H., and Muller, L. P. (1951). *Arch. Surg.*, 63, 379.
Blain, A. W., and Blain, A. (1950). *Ann. Surg.*, 131, 92.
Blakemore, A. H. (1951). *J Amer. med. Ass.*, 145, 1335.
— (1952). *Surg. Gynec. Obstet.*, 94, 443.
[illegible] 134, 420.
[illegible] : 701.
Cain, J. C., Grindlay, J. H., Bollman, J. L., Flock, E. V., and Mann, F. C. (1947). *Surg. Gynec. Obstet*, 85, 559.
[illegible] 22.
[illegible] 4, 521.
[illegible] 5, 407.
[illegible] 572.
Gerrard, J. (1952) [illegible]

[illegible], H. K. (1951) *Ann. R. Coll. Surg. Engl.* 8, 354

mer. med. Ass.,
138, 543
Pattison, A. C. (1949). *Arch. Surg.*, 58, 590.
Phemister, D. B., and Humphreys, E. M. (1947) *Ann. Surg.*, 126, 397.
Rienhoff, W. F. (1951) *Johns Hopk. Hosp. Bull.*, 83, 358.
Rosenbaum, D., and Egbert, H. L. (1952). *J. Amer. med. Ass.*, 149, 1210
Rousselot, L. M. (1952) *Surgery*, 31, 433.
Rowntree, L. G., Zimmermann, E. F., Todd, M. H., and Ajac, J. (1947). *J. Amer. med. Ass.*, 135, 630.
Satinsky, V. P. (1948) *Ann. Surg.*, 128, 938
Seneviratne, R. D. (1950) *Quart. J. exp. Physiol.*, 35, 77.
Smythe, C. M., Fitzpatrick, H. F., and Blakemore, A. H. (1951). *J. clin. Invest.*, 30, 674
Stock, F. E. (1952) *Ann. R. Coll. Surg. Engl.*, 10, 187.
Tanner, N. C. (1950) *Proc. R. Soc. Med.*, 43, 147.
Theron, P. (1953) *S. Afr. med. J.*, 27, 73.
Tidy, H. (1952) *Brit. med. J.*, 2, 1.
Walker, R. M. (1952) *Lancet*, 1, 729
— Middlemiss, J. H., and Nanson, E. M. (1953) *Brit. J. Surg.*, 40, 392.
Walshe, J. M. (1953). *Lancet*, 1, 1075.

RETINAL DETACHMENT: IMPROVEMENTS IN INVESTIGATION AND TREATMENT

By G. W. BLACK, M.B., B.S.(Lond.), F.R.C.S (Eng.).
Ophthalmic Surgeon, United Leeds Hospitals

The foundations of the present treatment of detachment of the retina remain those laid down by Jules Gonin, the Lausanne ophthalmic surgeon, whose lifetime's labour was devoted to this subject, from the publication of his *Recherches Anatomiques* in 1904, until his death in 1935.

He demonstrated (1) that the retina tears at a degenerate or atrophic focus, usually near its anterior border, (2) that fluid from the vitreous body passes through this tear, dividing the retina into its primitive layers, and (3) that for cure it is necessary to create a solid adhesion between the retina and the choroid, both at the site of the tear and in the surrounding area. All operations on detachment of the retina today are based upon these principles, but improvements have been made during the past few years, both in the investigation of cases and in their operative treatment. This progress may be summarized as follows.

(1) Improved methods of ophthalmoscopy.

(2) Emergence of a more precise understanding of the role of the vitreous body.

(3) Recognition of the importance of the choroid (*a*) in the absorption of subretinal fluid, (*b*) in the production of exudation as a result of treatment, and (*c*) in the occasional spontaneous repair of detachment.

(4) Improvements in methods of treatment, notably by scleral resection.

OPHTHALMOSCOPY

Finding the tear

In a detachment the discovery of the tear is indispensable to the rational treatment of the condition, and methods used to facilitate research into this factor contribute towards success. Gonin (1934) even designated the ophthalmoscope as the chief instrument for curing detachment of the retina.

Success in finding tears depends upon corneal transparency, a large clear pupil and the method of ophthalmoscopy employed.

Corneal transparency

Corneal transparency is especially important during any operation, to enable the operator constantly to check the effects of his treatment by direct reference to the fundus. The surgeon has often to accept corneal opacities, together with those of the lens, which inevitably restrict his field of view of the interior of the eye; but he should not contribute to his difficulties by allowing the cornea to lose transparency during the course of his operation.

Cocaine impairs corneal transparency and is unnecessary in the preparation of the patient for operation. A few drops of Guttae Holocainae (phenacaine hydrochloride) at 1 per cent, initially, to secure mild surface anaesthesia, allows the introduction of a needle into Tenon's capsule and infiltration with Novocain (procaine hydrochloride) 2 per cent, over the area of operation.

The most important way of preserving the transparency of the cornea is to ensure that it is covered by the eyelids during phases of the operation when the ophthalmoscope is not being used. This is possible only if the usual eye speculum is discarded. The rotation of the eye is facilitated by the omission of this instrument, and exclusion of the cornea from the field of operation is achieved. Retraction of the lids and eyeball is secured by suitably placed sutures, and when the cornea is exposed an assistant should frequently spray saline solution upon it.

Mydriasis

Maximal mydriasis is required to obtain the farthest anterior view of the retina by any method of ophthalmoscopy and can be obtained by injection of 5 minims of Mydricain, the formula of which is as under:

[illegible] Sulphate (B.P.)	0 03 gramme
[illegible]	0·18 gramme
[illegible]	3⅓ minims
Normal saline solution .	2½ minims
Chlorbutol (B.P.) . . .	0 02 gramme
Distilled water	to 10 minims

General effects from this injection rarely or never occur, and extreme mydriasis is obtained.

Methods of ophthalmoscopy

Direct method

British surgeons have relied in the main upon various excellent electrical ophthalmoscopes, using the direct method. There has been a renewal of interest in indirect [illegible] the past few years because the retina can be examined some- [illegible] fundus [illegible] emmetropic eye, but that only two-thirds of the total surface of the retina can be seen by this method. He also mentions that, in a statistical study of 400 consecutive cases of retinal detachment, it was found that out of all retinal breaks which could be detected by the use of his indirect binocular ophthalmoscope, only 41 per cent were detectable by using a direct ophthalmoscope.

[illegible] third of the retina is not visible by the direct [illegible] dilated to allow inspection almost to the ora serrata; this can be confirmed in those cases that have a coloboma of the iris, through which a view of the ciliary body can be obtained, and a comparison made between the anterior view obtained through the coloboma and through the intact pupil

Indirect method

However, while it is accepted that a zone of retina slightly anterior to the limits of view by the direct method can be obtained by the indirect method, the scale of lesions seen by this method is only one-third the size of that by the direct method. The indirect method requires strong illumination, but when it is recalled that some tears are no larger than the width of a retinal vessel, it will be realized that such tears may be smaller than the resolving power of the indirect method.

Trantas' method.—Some assistance in finding and elucidating tears in the extreme periphery may be obtained by using the method of Trantas (1900) This consists in

RETINAL DETACHMENT: IMPROVEMENTS IN INVESTIGATION AND TREATMENT

By G. W. BLACK, M.B., B.S.(Lond.), F.R.C.S.(Eng.).
Ophthalmic Surgeon, United Leeds Hospitals

The foundations of the present treatment of detachment of the retina remain those laid down by Jules Gonin, the Lausanne ophthalmic surgeon, whose lifetime's labour was devoted to this subject, from the publication of his *Recherches Anatomiques* in 1904, until his death in 1935.

He demonstrated (1) that the retina tears at a degenerate or atrophic focus, usually near its anterior border, (2) that fluid from the vitreous body passes through this tear, dividing the retina into its primitive layers, and (3) that for cure it is necessary to create a solid adhesion between the retina and the choroid, both at the site of the tear and in the surrounding area. All operations on detachment of the retina today are based upon these principles, but improvements have been made during the past few years, both in the investigation of cases and in their operative treatment. This progress may be summarized as follows.

(1) Improved methods of ophthalmoscopy.

(2) Emergence of a more precise understanding of the role of the vitreous body.

(3) Recognition of the importance of the choroid (*a*) in the absorption of subretinal fluid, (*b*) in the production of exudation as a result of treatment, and (*c*) in the occasional spontaneous repair of detachment.

(4) Improvements in methods of treatment, notably by scleral resection.

OPHTHALMOSCOPY

Finding the tear

In a detachment the discovery of the tear is indispensable to the rational treatment of the condition, and methods used to facilitate research into this factor contribute towards success. Gonin (1934) even designated the ophthalmoscope as the chief instrument for curing detachment of the retina.

Success in finding tears depends upon corneal transparency, a large clear pupil and the method of ophthalmoscopy employed.

Corneal transparency

Corneal transparency is especially important during any operation, to enable the operator constantly to check the effects of his treatment by direct reference to the func [illegible] opacities, together with those of the lens. [illegible] terior of the eye; but he should not [illegible] ea to lose transparency during the course of his operation.

Cocaine impairs corneal transparency and is unnecessary in the preparation of the patient for operation. A few drops of Guttae Holocainae (phenacaine hydrochloride) at 1 per cent, initially, to secure mild surface anaesthesia, allows the introduction of a needle into Tenon's capsule and infiltration with Novocain (procaine hydrochloride) 2 per cent, over the area of operation.

apposition of the shrunken vitreous body to the retina, should this become attached to the choroid, as it must to obtain a cure. More frequently the retina fails to become adherent to the choroid. The retina appears to require to be sandwiched between a resilient and intact vitreous and a choroid so treated as to produce an inflammatory exudate on its inner surface, which will lead to a firm fibrous adhesion between the layers.

Effects of operations for cataract

The function of the vitreous is illustrated by the claim made by Lister (1951) that the risk of detachment of the retina is greater after extracapsular than intracapsular extraction of cataract. This is said to be due to the needling operations on the residual capsule of the lens, which are frequently necessary to produce a clear pupil. As a result the vitreous herniates into the anterior chamber, and lines of traction are caused, which may act upon widespread delicate adhesions between the vitreous and focal

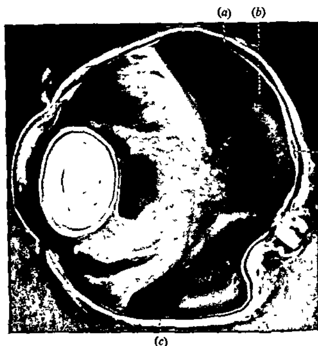


FIG. 126—Section of eye showing attachments of shrunken and detached vitreous to ciliary body and to the optic disc, (a) detachment of retina due to artefact, (b) pre-retinal cavity, (c) blood clot. (*By courtesy of Mr Eugene Wolff*)

points of atrophy or degeneration in the retina, and pull it off Such focal points are commonly present in eyes prone to detachment of the retina. However, many aphakic detachments arise after perfectly executed intracapsular operations, this is not surprising, for the unstable state of the face of the vitreous and the tremulous appearance of the iris on movement of the eyeball indicate the possibility that traction effects may be transmitted backwards through the vitreous to the retina Schepens (1951) found that, out of 83 aphakic detachments, 72 followed intracapsular operations and 11 extracapsular extraction. These figures do not give a true comparison, because, as he points out, the intracapsular operation is probably much more frequently performed in the United States of America. At least they render doubtful the view that there is a greater liability to retinal detachment after extracapsular extraction.

These observations may be summarized by laying stress upon the importance of a minute pre-operative examination of the vitreous, and of making every effort to conserve its substance.

Furthermore, it has often been noticed that when much solid vitreous has been lost in the course of a detachment operation, the detachment may be more ballooned and

indenting the sclera at the limbus with a glass rod, in order to cause infolding of successive areas of the retina to expose a tear not visible by other means. The method is not readily applicable to direct ophthalmoscopy. Experts in its use state that adverse effects have not been noticed, but there might be a disadvantage in causing deformation of the ora serrata in an eye predisposed to retinal tears.

Combination of direct and indirect methods

In summary, it is necessary to explore a retinal detachment by both methods: to obtain a conspectus of the detachment and a view of the extreme periphery of the retina by the indirect method, and a more intimate and detailed study of individual lesions by the direct method.

THE ROLE OF THE VITREOUS IN DETACHMENT OF THE RETINA

The base of the vitreous body is attached to the ciliary epithelium in a zone 1·5 millimetres broad, immediately anterior to the ora serrata. It is also adherent to the optic disc, but not normally to the retina. The vitreous body lies in close contact with the retina, and may become attached to it at foci of choroido-retinal inflammation or degeneration.

Examination with the slit-lamp

The vitreous body is described as an elastic hydrophilic gel, made up of a network of fibrillar micellae composed of a protein, called vitrein, enmeshing a viscous jelly of hyaluronic acid, the whole being permeated by the intra-ocular fluid (Duke-Elder, 1951).

Clinical observation of the vitreous in the dark room, and during the course of operations for cataract, provides evidence of great variation in its characters: volume, light transmissibility and texture. It has for long featured in the theories of the causation of detachment of the retina, but only in recent years has a much more careful assessment of the state of the vitreous become possible by the advance of slit-lamp microscopy. This has been brought about by the use of a new component for the slit-lamp microscope, the Hruby lens, which allows binocular examination of the vitreous and retina by means of a thin optical section (Hruby, 1941).

Detachment of the vitreous

It is now clear that in some cases of detachment of the retina there is a concurrent detachment of the vitreous body from the retina. This vitreous detachment, due to shrinkage of its substance, may precede and determine the onset of the retinal detachment. The retractile nature of the vitreous has often been noted by ophthalmoscopic observation in the presence of tags of retina, withdrawn into the vitreous from tears in the retina, and lying markedly internal to the plane of the detached retina.

By slit-lamp examination it is possible to detect relatively large cystic spaces between the vitreous substance and the retina, which may or may not itself be detached.

Fig. 126 shows marked retraction of the vitreous, with its basal and posterior attachments to the wall of the eyeball intact. The space between the retina and vitreous was, in this case, filled with blood On the temporal side there is a shallow separation of the retina, which may be post-mortem in character.

The interval between the vitreous and retina is normally filled by an aqueous fluid. The shrinkage of the vitreous must deprive the retina of its supportive and cushioning effect. If some small injury occurs to such an eye, this labile fluid from the cleft between the vitreous substance and the retina passes freely through the tear and detaches the retina. The evacuation of this fluid in the course of treatment cannot lead to the

Development of scleral resection

Scleral resection as a method of treatment does not belong to the Gonin tradition. It was first reported on by Müller in 1903 as a method of treatment for detachment of the retina in high myopia. His method consisted in excising an oval piece of sclera on the temporal side of the eyeball after resection of the external rectus muscle. The edges of the sclera were sutured, and the eyeball was flattened on this aspect and shortened. It is remarkable to find that he obtained 6 cures in 19 cases—a high percentage in comparison with other empirical methods of treatment used at that time. It should be recalled also that de Blaskovics (1911) modified this method of full-thickness sclerectomy by leaving a lamella of sclera next to the choroid.

Borley (1949) has collected a total of 82 operations performed by these early authors and others. Cures were claimed for 18 cases (approximately 22 per cent) and improvements in 24 cases (30 per cent).

The world-wide interest in Gonin's report on his treatment of detachment, given at the International Congress of Ophthalmology at Amsterdam in 1929, caused interest in scleral resection to disappear.

This method was revived by Lindner in 1931 and reported upon by him in 1933 (Lindner, 1949). He performed a perforating sclerectomy, removing a strip of sclera 2–6 millimetres wide and 20–35 millimetres long, but it cannot be said that he had many followers at this time.

It is only during recent years that surgeons in increasing numbers have used this method of treatment in their most grave and apparently hopeless cases, in many of which the patients have had a series of unsuccessful operations, and in which the early topography of the detachment has been lost in extensive pigmentary changes and choroidal atrophy; the vitreous is often hazy and the search for a tear usually fruitless. As a consequence, scleral resection is often the terminal treatment in the most unfavourable cases

Methods of scleral resection

Scleral resection is a difficult and laborious technique. It cannot yet be regarded as a fully established procedure, being still in the process of development. The earlier workers (as is noted above) removed full-thickness strips of sclera, and this method is still practised by some surgeons Recently, partial-thickness or lamellar excision has been revived Weve (1952) prefers reefing of the sclera, combined with diathermy; his method consists (1) in passing an inert suture through the superficial layers of the sclera, in purse-string or criss-cross pattern, around the area of diathermy, (2) in evacuation of subretinal fluid, and (3) in tightening of the suture to cause a localized flattening or infolding of the choroid and retina. All these methods reduce the capacity of the eyeball, shorten it, alter the curvature of the cornea in some degree, and aim at providing apposition of the choroid and retina to a reduced or shrunken vitreous. Hence the need of careful estimation, by means of the slit-lamp and Hruby lens, of the approximate size of the vitreous body and of the depth of the detachment of the vitreous, if this is present, and of the assessment of the width of scleral resection needed to fit the reduced sclera to the vitreous.

Perforating (full-thickness) scleral resection

The conjunctiva is incised and one rectus muscle is divided (Figs. 127 and 128). The proximal end of the muscle is held by a suture. The sclera is carefully exposed by the removal of episcleral connective tissue, and a haemostatic field is obtained by the [illegible]

[illegible] with a

[illegible] nterior

extensive after operation. This is due to the drift of the vitreous towards the point of evacuation, and to the consequent pulling off of the retina on the opposite side of the globe.

THE IMPORTANCE OF THE CHOROID

Every case of detachment of the retina requires a period of expectant treatment, which gives time for the necessarily laborious investigation to be carried out, and also permits of a study of the probable function of the choroid in the absorption of the fluid which separates the layers of the retina.

The choroid in spontaneous cure of retinal detachment

In 7 of a recent series of 100 cases of retinal detachment treated by the writer, rest in bed alone and the use of eye-pads were sufficient to lead to a full and permanent replacement of the retina. This is not an insignificant percentage, and these spontaneous cures were spread over cases with and without visible tears in the retina; such cures depend largely upon two factors: (1) the tendency of the choroid to absorb the fluid which passes from the vitreous through the torn retina, and (2) the tendency of the choroid at the same time to develop an irritative inflammatory reaction, which *may be sufficient to cause adhesion between the layers of the retina and itself.* Such a reaction in the choroid is often depicted by a line of pigmentary change, which is seen at the limits of spread of a detachment that has undergone a spontaneous cure. Where the choroid possesses a good body and colour, and is free from atrophy or gross pigmentary change, or if the retina subsides markedly as the result of the absorption of fluid after a few days' rest in bed with the use of pads, the prospects of surgical replacement of the retina are good. Such a choroid is capable of pre-operative absorption of fluid, of responding by forming an exudate on its inner surface as a result of diathermic or chemical applications to its outer surface, and finally of absorbing any excess of exudate produced by these methods of artificially induced choroiditis, which is the desired effect of these adhesive methods of treatment.

Operative damage.—These operations must be carefully devised to avoid too much damage to the choroid. This is apt to occur in cases in which tears are not discovered [illegible] unseen tears [illegible] oo severe [illegible] iatory reaction, thrombosis of the vorticose vein and ultimate gross choroidal atrophy, without securing replacement of the retina.

SCLERAL RESECTION

Comparison with other methods

It must be emphasized that this method of treatment, which has lately received some attention, is no substitute for the standard procedures which have been well tested over the past 25 years by many ophthalmic surgeons, and are not described in any detail in this article. Suffice to say that methods of treatment, depending upon tissue coagulation by diathermy, electrolysis or caustic potash, all have their advocates.

Diathermal and chemical coagulation.—Diathermy is certainly the most popular [illegible] methods of chemical coagulation [illegible] *id to create* an ad- [illegible] be remembered in any history of the surgery of detachment of the retina.

Development of scleral resection

Scleral resection as a method of treatment does not belong to the Gonin tradition. It was first reported on by Müller in 1903 as a method of treatment for detachment of the retina in high myopia. His method consisted in excising an oval piece of sclera on the temporal side of the eyeball after resection of the external rectus muscle. The edges of the sclera were sutured, and the eyeball was flattened on this aspect and shortened. It is remarkable to find that he obtained 6 cures in 19 cases—a high percentage in comparison with other empirical methods of treatment used at that time. It should be recalled also that de Blaskovics (1911) modified this method of full-thickness sclerectomy by leaving a lamella of sclera next to the choroid.

Borley (1949) has collected a total of 82 operations performed by these early authors and others. Cures were claimed for 18 cases (approximately 22 per cent) and improvements in 24 cases (30 per cent).

The world-wide interest in Gonin's report on his treatment of detachment, given at the International Congress of Ophthalmology at Amsterdam in 1929, caused interest in scleral resection to disappear.

This method was revived by Lindner in 1931 and reported upon by him in 1933 (Lindner, 1949). He performed a perforating sclerectomy, removing a strip of sclera 2–6 millimetres wide and 20–35 millimetres long, but it cannot be said that he had many followers at this time.

It is only during recent years that surgeons in increasing numbers have used this method of treatment in their most grave and apparently hopeless cases, in many of which the patients have had a series of unsuccessful operations, and in which the early topography of the detachment has been lost in extensive pigmentary changes and choroidal atrophy; the vitreous is often hazy and the search for a tear usually fruitless. As a consequence, scleral resection is often the terminal treatment in the most unfavourable cases

Methods of scleral resection

Scleral resection is a difficult and laborious technique. It cannot yet be regarded as a fully established procedure, being still in the process of development. The earlier workers (as is noted above) removed full-thickness strips of sclera, and this method is still practised by some surgeons Recently, partial-thickness or lamellar excision has been revived. Weve (1952) prefers reefing of the sclera, combined with diathermy; his method consists (1) in passing an inert suture through the superficial layers of the sclera, in purse-string or criss-cross pattern, around the area of diathermy, (2) in [illegible]

providing apposition of the choroid and retina to a reduced or shrunken vitreous. Hence the need of careful estimation, by means of the slit-lamp and Hruby lens, of the approximate size of the vitreous body and of the depth of the detachment of the vitreous, if this is present, and of the assessment of the width of scleral resection needed to fit the reduced sclera to the vitreous.

Perforating (full-thickness) scleral resection

The conjunctiva is incised and one rectus muscle is divided (Figs. 127 and 128). The proximal end of the muscle is held by a suture. The sclera is carefully exposed by the removal of episcleral connective tissue, and a haemostatic field is obtained by the cauterization of bleeding points, when necessary.

The parallel strip, with pointed ends for excision, is defined by a line made with a series of light diathermy applications, or with a solution of methyl violet. The anterior

Partial-penetrating (or lamellar) scleral resection

In this modification, access to the sclera is obtained as in the previous method. The site of resection is outlined, and the knife is carefully carried down almost to the choroid at one end of the strip (*see* Figs 129–134).

A traction suture is inserted, and delicate strokes of the knife are used to raise the scleral flap, leaving a thin lamella to enclose the choroid. This method is more speedy than performing scleral resection, and the strip can be entirely removed before the stitches are inserted. It is customary, after the removal of the segment of sclera, to apply a blunt diathermy electrode lightly to a number of points along the borders of the cleft in the sclera, in order to enhance the effect of the eye-shortening procedure. For the same reason, some surgeons have applied caustic potash to the thin lamella of sclera which covers the choroid. After these applications, stitches are inserted into the edges of the wound, the subretinal fluid is evacuated, and the stitches are tightened to cause an infolding of the scleral lamella and the choroid.

Indications for operation

Aphakia.—In general the treatment of detachment in aphakia is the same as that of other types of the condition. Scleral resection is the method of choice in cases in which there has been much vitreous loss at the time of extraction of a cataract, or the pupil is obscured by the lens capsule, or no hole can be found.

Vitreous strands and retinitis proliferans.—As a result of perforating injuries, infection may be carried into the eye and intra-ocular haemorrhage may occur. These complications may be followed by the formation of vitreous strands and of a fine sheet of pre-retinal fibrous tissue. A contraction of this fibrous tissue may drag off the retina from the choroid, causing an essential shrinkage of the retina and a disproportion in size between it and the scleral envelope This may be corrected by scleral resection.

Non-response to surgical treatment.—Scleral resection is also indicated where no response has been effected by other operative measures.

Results of scleral resection

Full-thickness resection

Shapland (1952) lists 158 cases of full-thickness resection performed by various surgeons, in which 29 per cent of patients were cured and 22 per cent improved. It is assumed that a "cure" refers to an anatomical replacement of the retina with varying visual results, and that "improvement" refers to partial replacement of the retina, some improvement in visual acuity and in the field of vision having been secured.

Lamellar resection

Shapland (1952) has been the chief advocate in Great Britain of lamellar resection, and he has published a series of 36 cases in which 11 patients were cured and 10 were improved. These results compare with those of other workers. They were obtained in a group of cases which were hopeless when treated by other methods.

The operations can be repeated, and usually cause little local reaction. It may be, however, that "successful" scleral resections today may need to be repeated in the course of the next few years, if further shrinkage of the vitreous takes place. Such a development might entail a refitting of the sclera to the vitreous.

Conclusions

The results of the perforating and non-perforating methods appear to be similar, but the latter method is easier to perform, involves less risk to the choroid and vitreous, and to the writer seems likely to become the method of choice.

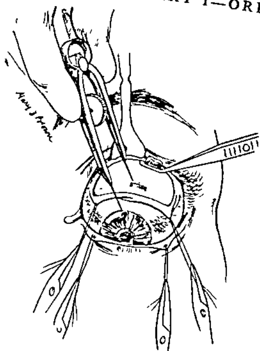


FIG. 129.—Calipers in position defining anterior border of lamellar resection.

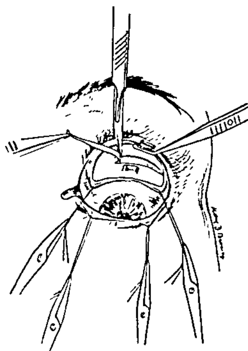


FIG. 130.—Elevation of lamella.

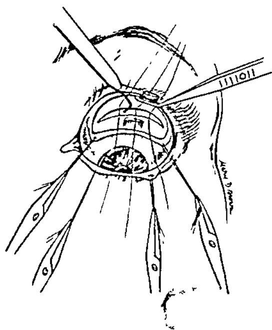


FIG. 131.—Diathermy electrode applied f evacuation of inter-retinal fluid.

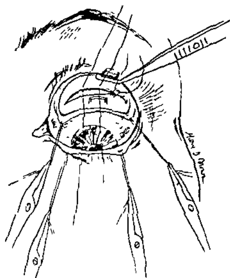


Fig. 132.—Suture of margins of sclera and infolding of lamella.

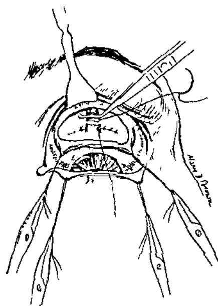


Fig. 133 —Suture of superior rectus muscle

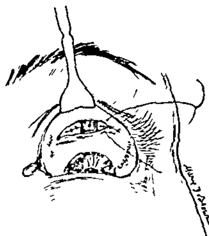


Fig 134 —Suture of conjunctiva.

(*See also British Surgical Practice:* Retina, Vol. 7, page 407, S. Key 296)

REFERENCES

de Blaskovics, L. (1911). *Szemeszet* (No. 2).
Borley, W. F. (1949). *Trans. Amer. Ophthal. Soc.*, 47, 462.
Duke-Elder, W. S. (1951) *Recent Advances in Ophthalmology*, 4th ed. London; Churchill.
[illegible]
[illegible]
Lindner, K. (1949). *Arch. Ophthal., Chicago*, 42, [illegible]
Lister, A. (1951). *Trans Ophthal. Soc. Aust.*, 11, 39.
Muller, L. (1903) *Klin Mbl. Augenheilk.*, 41, 459.
Schepens, C. L. (1951). *Trans Amer Acad.*, July-August.
Shapland, C. D. (1952). *Trans. Ophthal Soc. U.K.*, 72, 119.
Trantas, A. (1900) *Arch. Ophtal*, *Paris*, 20, 314.
Weve, H. (1952) *Irish J. med. Sci.*, 6th series, 74.

BIOLOGICAL DECORTICATION
(ENZYME DEBRIDEMENT)

By T HOLMES SELLORS, D.M., M.Ch, F.R.C.S.
Senior Surgeon, the London Chest Hospital and Harefield Hospital;
Thoracic Surgeon, the Middlesex Hospital

INTRODUCTION

It has been recognized for a number of years that haemolytic streptococci produce extracellular enzymes which have a fibrinolytic action. This can be simply demonstrated by adding a broth culture to human blood clot which is then broken down into a uniform liquid Streptococcal infections, moreover, are often characterized in the early stages by the absence of fibrinous barriers as compared, for example, with staphylococcal or pneumococcal processes.

The clinical aspect of this phenomenon has recently found application in cases of enclosed blood clot, notably clotted haemothorax, and in examples of chronic suppuration Enzymes derived from haemolytic streptococci, named streptokinase and streptodornase, can be applied to the affected surface or cavity, and the fibrinolytic action helps in the removal of unwanted debris and renders fibrin masses more soluble and liquid. The pancreatic enzyme, trypsin, has also been used in similar circumstances, but here the action is proteolytic rather than fibrinolytic The essential feature of both types of agent is that their solvent action takes place on extracellular deposits and not on living cells themselves.

METHOD OF ACTION

Much of the pioneer work on the fibrinolytic action of haemolytic streptococci has been carried out by Tillett and his associates (1951), who have studied this problem for the past 20 years Examination of the different groups of haemolytic streptococci has shown variation in the activity of the fibrinolysis. Out of 285 strains of Lancefield Group A 98 per cent were fibrinolytic, and in Group G 70 out of 70 were similarly active. On the other hand, Groups B, D, E, F and H were inert. The organism finally selected for the production of enzymes was Group C, strain H 46 A, because it is sufficiently active and yet almost non-pathogenic for man.

The active substance in this case appears to have a specific action on fibrin and does not resemble the proteolytic enzymes produced by many other organisms. The action is not direct, however, for if this extract is added to clot formed by pure fibrinogen and thrombin lysis does not occur. Some additional human serum factor is needed for reaction; this is found in the euglobulin moiety of plasma protein, and is referred to as plasminogen Plasminogen is present in blood and body exudates and can be activated by the streptococcal extract to form the enzyme plasmin whose action on fibrin is direct The activator of this enzyme has been named streptokinase (SK); and this can be suitably prepared and standardized

The effect of streptokinase on fibrin is to break down the insoluble protein into polypeptides which are soluble. The liquefaction depends on the extent to which the injected streptokinase can diffuse through the clotted mass and activate available plasminogen into plasmin. The substance is most efficient between *p*H ranges of 7·5–7·6 and is ineffective beyond *p*H 5 and *p*H 9.

It has also been determined that purulent material can be liquefied by the addition of streptococcal exudate, though in this cases the process is due to a specific active enzyme, streptodornase (SD). The viscosity of pus is due to the presence of a nucleoprotein—desoxyribonucleoprotein—with its corresponding nucleic acid, which accounts for 30–70 per cent of the coarse sediment of pus. Streptodornase, which is freely found in streptococci of the Lancefield Group B, produces the breakdown of the complex nucleoprotein into simpler and more soluble molecules. It does not require the presence of a serum factor and has the merit of acting only on extracellular nucleoprotein.

Streptodornase, when added to pus, converts a thick heavy mass into a milky fluid of low viscosity within a short space of time. The sediment has been recorded as being reduced from 70 to 23 per cent within an hour, while the viscosity fell in the same period from 100 to 4. The breakdown of desoxyribonucleoprotein occurs with formation of nucleotides and nucleosides, and final reduction to purines and pyrimidines The effective *p*H is the same as for streptokinase, but citrates are known to nullify the action of streptodornase.

The enzyme, trypsin, has a powerful proteolytic action which is effective on protein, including mucin and fibrin, breaking them down into polypeptides and amino acids Living cells are protected from its destructive action by the presence of a specific inhibitor which may be related to antiplasmin.

Trypsin, though stable in crystalline form, rapidly loses its efficacy in solution. It has been estimated that three-quarters of its value is lost in 3–4 hours. It is most active at a *p*H range of 7, and, as with preceding substances, it is useless beyond the ranges of *p*H 5 and 8.

The influence of the hydrogen ion concentration on the enzymes makes it imperative to determine the reaction of the clot or pus that is to be acted upon. Pus as a rule is acid, and the *p*H can usually be estimated by nitrazine paper, after which the use of a buffer solution to bring the pus within a suitable range can be considered. Sorensen's phosphate buffer solution is an appropriate agent in most cases, but in the case of clotted fibrin masses the testing of reaction and its adjustment is not straightforward. Fortunately, the reaction of fibrin and clot is usually within the range of the enzyme activity.

One of the most striking effects of enzyme activity on pus and necrotic tissue is the way in which the underlying viable tissues show a favourable response to the removal of pus and debris from its surface. A dull sodden surface becomes fresh and glistening, and an active exudate is extruded which has both a mechanical flushing effect as well as providing a fresh supply of antibodies to combat infection. It is probably for this reason that chronically infected surfaces and cavities become bacteriologically clean after the use of these enzymes alone, though the use of topically applied antibiotics is by no means precluded. One danger from the production of an exudate in an enclosed space is an increase in pressure which must be relieved by aspiration. At the same time as the cleaning process—sometimes referred to as enzymatic debridement—is taking place, there is the formation of active granulation tissue, which is responsible for some degree of blood-staining of the effusion. If treatment is initiated shortly after operation, or when active ulceration is present, there is a risk that healing may be jeopardized by the removal of fibrin from raw surfaces. This has been regarded as a real danger in pulmonary resection, where the organization of fibrin into fibrous tissue plays a valuable part in the healing of the divided bronchus stump.

The solvent action of streptokinase and trypsin on loose fibrin is recognized, but once fibrin has become organized into firm fibrous tissue the enzymes have no effect. The clinical application of this is important in pleural infections where the fibrin deposit on pleural surfaces becomes organized into a thick fibrous layer, which persists and resists solvent action.

DOSAGE AND METHOD OF APPLICATION

Dosage

In practice it has been found convenient to use streptokinase (SK) and streptodornase (SD) together in a proportion of 4 to 1. Streptokinase is effective in a dose of 80,000–450,000 units, but works best in a dilution of 1 in 32. A standard injection consists of 100,000 units SK and 25,000 units SD, which is freshly prepared in 10–20 millilitres of sterile saline solution. If it is possible to make any calculation of the volume of the area to be treated the optimum dilution should give, according to Tillett and his co-workers (1951), 10,000 units SK and 4,000 units SD per millilitre.

Trypsin should be used only in freshly made up solutions, and, indeed, where possible, should be used as a powder on free surfaces which have been irrigated with a phosphate buffer solution. An average dose is 250,000 Armour units dissolved in 25 millilitres of buffer solution. The trypsin unit is based on the decomposition of haemoglobin into a hydroxyaryl compound, which can be treated with a reagent that allows it to be contrasted colorimetrically with tyrosine; 1,000 units are equivalent on this basis to one milligram of tyrosine.

Method

In the case of fibrin clot, SK-SD or trypsin solution is injected into the mass and the resultant liquid aspirated as completely as possible 24 hours later. If the clot is extensive, one or more further injections will be required into different sites until the whole mass is liquefied. Efficient aspiration is essential to the success of treatment. In the case of an extensive clotted fibrino-haemothorax, two or three injections are usually required, but the first injection should not be made too soon after the onset of the haemorrhage, in case solution of the clot leads to further active bleeding.

With enclosed collections of pus, the procedure is to aspirate and wash out the space as thoroughly as possible and then to inject SK-SD or trypsin solution in appropriate dosage; aspiration is performed the next day. The following day a further injection is given with aspiration again 24 hours later There must be no delay in the injection and aspiration sequence, since delay leads to the production of anti-enzymes in the space, which reduce the efficiency of the lysis.

Thick pus becomes much thinner after the first injection, and less opaque with subsequent injections In many cases the aspirated fluid is clear in 4 or 5 days and bacteriologically sterile, though blood-staining is a common though unimportant f [illegible] l examination should be made, [illegible] they are not always necessary. [illegible] 24 hours, and it is important to wash out the space thoroughly before each instillation.

In the case of open wounds and sinuses the enzymes can be used for irrigation, or in the case of trypsin by actual dusting of the powder on the raw surfaces. The action can be compared with that of Dakin's solution in producing a chemical debridement. This, however, is effective for only a short time, while the enzyme action is more prolonged, though it requires reapplication at frequent intervals. Dusting with trypsin powder should be repeated every 15–30 minutes, to avoid the production of inhibiting agents and to replace the powder that is washed away by the exudate. The patient often encounters a stinging sensation or local pain during the treatment. Irrigation or wet dressings of SK-SD solution have the same effect and can be prepared, using 20,000 units SK and 5,000 units SD in 3 or 4 millilitres of saline.

The use of trypsin intravenously has been considered in the treatment of [illegible] thrombotic cond [illegible] wise might prod [illegible] monary embolism and similar conditions have been suggested as suitable indications

for the careful use of this agent. A dosage of 100,000–200,000 units is suggest given at a rate of 25–30 drops per minute; the injection can be given once o day with a maximum dose of 750,000 units during four days. Euphoria is oft as a result of the injections, even though there may be a sharp constitutional This form of treatment should not be used in cases where there is any liver da the inhibitor of trypsin cannot be produced in adequate quantity.

The use of trypsin in aerosol solution has possibilities in cases where the is unduly tenacious If the trypsin is made up at a pH of 7·1 in a quantity of units per millilitre, the rate of inhalation should be at about one millilitr minutes A low starting dose is recommended, to be worked up to 100,000 the second day and twice this amount on the third. The sputum becomes mo and considerable cough with fluid expectoration can be expected.

Reactions

SK-SD solutions if injected into an enclosed space produce a definite consti reaction in many cases. A rise in temperature may be noted within 5 or 6 rising to a peak (101°–102° F.) in 24 hours, and then subsiding. General sometimes with nausea and vomiting, may occur, but this feature is usually tra Trypsin appears to produce a more rapid and sharp reaction, which can be co by one of the antihistamine preparations such as Benadryl, 25–50 milligram before the injection and repeated every three or four hours for three or four

Allergic reactions have been recorded, but they are rare and may have been pr by additional therapeutic agents. Reactions in general have become less c and less severe as the purification of the preparations has improved.

Contra-indications

These enzymes should not be used in the presence of a recent active haem or of acute inflammation. The solution of clot or barely formed fibrous barriers clearly dispose to further haemorrhage or spread of infection. Similarly, consi discretion should be used after operation for the same reasons.

Clinical application

The most valuable field for enzyme therapy lies within the chest; clotted [illegible] pleural infections and the complications of pulmonary resection p [illegible] nore diffuse field is in c [illegible] , and in the sinuses of c

Haemothorax

Since World War II considerable attention has been given to so-called c haemothorax which is said to occur in 70–75 per cent of all traumatic haemoth The term is misleading since it gives the impression that the blood which ordi [illegible] remained as a firm re [illegible]

goes ordinary clotting The rapid movements of the heart and lung [illegible] mass so that within a space of a few [illegible] a heavily blood-stained fluid is prod This fluid contains no fibrinogen, [illegible] rapidly develops in response t irritation of the blood. This effusi[illegible] dilutes the existing haemoglobin pleural cav[illegible] contains fibrin[illegible] may give a concentration up to level or [illegible] week or ten [illegible] It is this secondary appeara fibrinoge[illegible] the "clotte[illegible] more appropri be referr[illegible]

If early and efficient needle aspiration is employed the ordinary haemothorax can be cured within a space of days. Delayed treatment will run the risk of secondary clotting which makes aspiration impossible. It is these cases that constitute a problem if they come for treatment several weeks after the onset of the condition If lung function is to be regained, the clot must be removed and any fibrin deposit on the chest wall and lung removed to allow full re-expansion of the lung The operation of decortication gained considerable popularity during World War II, but no one would deny that it is a major undertaking.

Fibrinolytic enzymes have their most valuable role in being able to dissolve the clot so that it can be removed by simple aspiration without recourse to surgery. Solid masses, loculated collections and pockets can all be treated in this way with reasonable expectation of a good result, unless the chest wall is so fixed and "frozen" by organized fibrous tissue that it cannot be freed from this lining.

The average haemothorax should receive an initial injection of 200,000 units SK—50,000 units SD being optional—well into the clotted mass. Aspiration the following day will draw off a considerable quantity of liquid blood, and a radiograph will decide if further enzyme injection is required. Sometimes a posterior injection has to be followed by an anterior or lateral one to reach areas that were not liquefied by the first injection During injection and aspiration strict precautions must be taken to avoid admission of air, and the necessity for intensive physiotherapy with breathing exercises to obtain re-expansion of lung must not be overlooked.

Enzyme therapy should not be considered within 7–10 days of the injury This rarely applies to traumatic cases which are usually considered at a much later date, but it has a definite application in cases with post-operative haemorrhage after a thoracotomy. Too early use may lead to further bleeding.

Apart from intrapleural haematomas, there are other sites in the thorax which sometimes harbour a large and unwanted clot. After the operations of extrapleural pneumolysis and thoracoplasty with apicolysis, a large dead space is formed and reactionary haemorrhage into this may occur. Streptokinase has proved efficacious in liquefying the clot and allowing its withdrawal through a needle without recourse to opening up the wound for its evacuation.

Infected pleural effusions

(*a*) *Infected haemothorax* responds satisfactorily to the use of SK-SD and trypsin solutions. Fragmented clot and debris is dissolved, and antibiotics injected into the space can become effective against infective organisms. If thorough aspiration is combined with physiotherapy the condition may be cured without having to drain the pleural cavity

(*b*) *Post-pneumonic infections* have been considered suitable for enzyme therapy, but in spite of enthusiastic claims in certain instances this form of treatment should be regarded as supplementary to, rather than replacing, existing methods. The value of enzymes lies in their ability to dissolve fibrin masses and to render the contents less viscous so that they can be aspirated. Repeated aspiration used with antibiotics is an effective form of treatment in early pleural infections, but the ultimate failure of aspiration is usually due to the pus being too thick or the needle becoming blocked by fibrin flakes.

There is no necessity to use fibrinolytic agents in the early stages, and indeed they might be dangerous. The greatest assistance can probably be derived from their use in the second or third week. After three or four weeks the fibrin [illegible] the pleural surfaces has started to or[illegible] stances should the use of enzymes [illegible] uncontrolled, or if the empyema space is not steadily reducing in size.

(*c*) *Chronic empyema* can be considered according to whether the cavity is open or

closed. A closed and relatively uninfected space can be cleaned by injecting SK-SD solution and leaving it for 24 hours before aspirating. Repetition of the procedure on two or three occasions may leave a clean cavity lined with fresh granulation tissue, but this by itself will not close the space. A chronic empyema with a persistent drainage opening can be treated by four or five consecutive instillations of enzyme solution leaving the surface sinus plugged for 24 hours. Considerable improvement in the bacteriology of the cavity follows and the presence of a clear blood-stained discharge suggests the presence of fresh granulation tissue. The suggestion that the surface sinus should be allowed to close before the internal space is obliterated cannot be regarded with favour. Most cases require adequate drainage and physiotherapy before final healing occurs. Enzyme therapy plays its part in initiating the healing process after a prolonged period of delay.

Decortication or pleurectomy in the treatment of chronic empyema is indicated when the rigid fibrous walls are preventing the closure of the empyema. Enzyme therapy affords a satisfactory method of preparation in long-standing cases, but it is not the method of treatment for a thick fibrous-walled cavity. Infected dead spaces (Semb space) after thoracoplasty can be most troublesome and lead to sinuses along the scar. Marked improvement has been noted after using enzymes followed by streptomycin or other suitable antibiotics.

(*d*) *Tuberculous* empyema can similarly be assisted by the use of enzymes. Liquefaction of the contents and cleansing of the walls gives considerable improvement, but again, if the walls are thick and rigid it will have no effect on the mechanical side of the condition. In early cases of tuberculous invasion of the pleura the one real hope of cure lies in obtaining rapid expansion of the lung with obliteration of the pleural space. Though this can be achieved in some instances the fibrous barrier over the lung is a much more resistant and constricting membrane (constrictive pleurisy) than with pyogenic infections. Hypochlorite and azochloramide solutions have had some success, but the action of enzymes, notably trypsin, can be effective where the chemical decorticating agents have failed. Long-standing empyema will not close with any treatment short of surgery, but can be cleaned and prepared by enzyme injections. The occurrence of a broncho-pleural fistula during the debridement is a circumstance that should not be attributed solely to enzyme action. The ulceration may have already occurred and removal of a slough may open the fistula.

(*e*) *Pulmonary resection* affords a field in which the enzymes can be used with some advantage so long as their timing is carefully chosen. In the performance of segmental resection for tuberculous lesions of the lung there is a recognized risk of broncho-pleural fistula. This may arise from breakdown of the bronchus stump which may be invaded by tuberculous tissue, or from a persistent and uncontrolled alveolar leak. At the same time a certain amount of haemorrhage may occur from raw surfaces. If, in spite of suction drainage tubes, air persists within the pleural cavity, the remaining lung tissue will collapse and will gradually be covered by a layer of fibrin which, on organizing, will prevent apical expansion of the lung. This handicap is made worse by haemorrhage or active pleural effusion. If streptokinase is used before the condition becomes chronic the clot may dissolve and free the depressed lung surface. On the other hand, too early use of enzymes may interfere with normal healing and actually produce a broncho-pleural fistula as well as leading to secondary haemorrhage. It is unwise to use the agents within a week or ten days of the operation; their most effective time for action is between the second and third weeks before organization of fibrin takes place.

Chronic suppurative conditions

In the case of extensive surface ulceration with sloughs and chronic secondary infection there is scope for debridement by the action of enzymes which, in eliminating

necrotic tissue, help to produce a clean healthy surface of granulation tissue. In extensive burns the surface has on occasions been prepared more readily for grafting than would be the case with other methods. Similarly with pressure ulcers a clean surface is produced in a comparatively short time. If SK-SD is used they should be [illegible]

[illegible] considerable improvement after enzyme injection both in the quantity and quality of the discharge. Small pieces of necrotic tissue will be broken up and discharged, but large masses such as sequestra are not likely to be affected. Tuberculous sinuses when irrigated show a change from pale flabby granulation tissue into tracks with fresh pink edges.

The fibrinous exudate of tuberculous meningitis has been treated by streptokinase injections in conjunction with streptomycin, but the reactions encountered have given some doubt as to the efficacy of this treatment, though more purified forms of the enzymes are said to produce less reaction

(*See also British Surgical Practice*. Pleura—Diseases of, Vol. 7, page 55, S. Key 270)

BIBLIOGRAPHY

Cathie, I. A B. (1949) *Lancet*, **1**, 441
Christensen, L. R (1945) *J gen. Physiol.*, 28, 363
Dragstedt, C. A. (1943). *Science*, 95, 131
Garner, R L., and Tillett, W. S (1934) *J exp. Med*, 60, 239
[illegible]

THE SURGERY OF CORNEAL GRAFTS

By B. W. RYCROFT, O.B.E., M.D., D.O.M.S., F.R.C.S. (Eng.).
The Corneo-Plastic Unit and Eye Bank, Queen Victoria Hospital,
East Grinstead, Sussex

"*After ulcerſ of the cornea, which have been large, the inequalitieſ and opacity of the cicatrix obſcures the ſight; in thiſ caſe could not a ſmall piece of the cornea be cut out by a kind of trephine about the ſize of a thick briſtle, or a ſmall crow-quill and would it not heal with a tranſparent ſcar?*"

Erasmus Darwin,
Zoonomia, Pt. II, p. 48, 1796.

HISTORICAL SURVEY

The course of corneal-graft surgery has had three phases—Fantasy, Faith and Fact. Dieffenbach in 1831 surveyed contemporary attempts at corneal transplantation and stated that "L'idée qui consiste à replacer la cornée trouble d'un homme par la cornée claire d'un animal certe une fantasie audacieuse et serait le plus grand succés de la chirurgie si cette opération réussisait". He had the doubts of his day, for the eye surgeons of the nineteenth century had confusion of thought between heteroplasty and homoplasty. In addition, their instruments were crude, infection was rife and anaesthesia was necessarily imperfect since the local application of cocaine was not in general use until after 1888. There had been early trials with corneal inserts of glass and egg membrane, but these were always extruded or were complicated by infection and severe fibrosis. The stage of heteroplasty followed, using graft material from pigs, cats and dogs. Reisinger in 1824 was the first to perform successful animal keratoplasty, and undoubtedly stimulated interest throughout Europe. Nevertheless, successes were very few and decades of fruitless experimental keratoplasty followed.

Towards the end of the century attempts were made to graft animal corneas on to human eyes, and although there were reports of successful technique the graft was rarely of any use since it became opaque and merged with the scar tissue of the host cornea (Marcus, 1841, Feldman, 1844; Plouvier, 1845; Power, 1872, and Johnson, 1886). Von Hippel after ten years of experimental work, attempted to graft a piece of rabbit cornea on a human eye, and at the fifth attempt he was successful. The patient was exhibited at Heidelberg in 1886 and 1887, during which time the rabbit graft, which was of partial thickness, remained clear and there was some improvement in the patient's vision. About this time von Hippel had devised his special clockwork trephine which facilitated the excision of grafts, and he came to prefer the partial-thickness graft after a tragedy which had followed a full-thickness graft due to infection.

Zirm's case in 1905 marked the transition from the period of Faith to that of Fact. He transplanted a piece of a boy's cornea to that of a man who had been blinded by lime splash; von Hippel's trephine was used. Vision improved and was carefully recorded for two years until the patient died. As a result of his experience Zirm decreed certain conditions which he considered were essential to success, and with minor modifications they hold good today. The conditions were: (1) the exclusive use of a human donor as distinct from animal material; (2) safe anaesthesia, strict asepsis and the avoidance of antiseptics; (3) the protection of the graft in warm, steamed

gauze; (4) firm retention of the graft by cross sutures; and (5) selection of cases.

Thus the phase of Fact opened at the beginning of the present century. Typical reports of successful cases were those of Elschnig and the Prague School from 1914 to 1930 which recorded a large series with 20 per cent clear grafts and 43 per cent improved vision. Filatov (1934) drew attention to the donor graft and declared that cadaver grafts were equal to, if not better than, living grafts. By 1930 ideas of graft form and technique were becoming crystallized; homoplasty was firmly established and there were many reports of successful cases in different countries. Tudor Thomas introduced his bevel edge in Great Britain, while Castroviejo, in the United States of America, preferred the square graft. During World War II Franceschetti (1950) employed the skill of Swiss instrument makers to produce his adjustable trephine which is in common use today. In 1949 Paufique and his colleagues revived interest in the lamellar method of keratoplasty by their brilliant publication of *Les Greffes de la Cornée*. Recently in Spain, Barraquer and Arruga have stressed the importance of accurate fixation of the graft by direct sutures.

Keratoplasty now has a firmly established place in ophthalmic surgery for the treatment of blindness due to corneal disease.

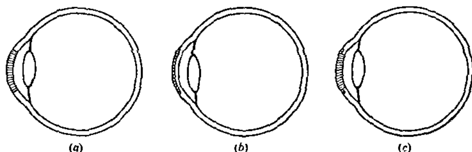


FIG 135.—(*a*) Full-thickness graft; (*b*) partial-thickness graft, (*c*) flange graft.

TYPES OF KERATOPLASTY

Increased experience during the last few years has improved the appreciation of the scope of keratoplasty and, briefly, the method of operation is governed by the area, depth and density of the corneal scar.

Full thickness, in which the eyeball is opened (Fig. 135*a*)

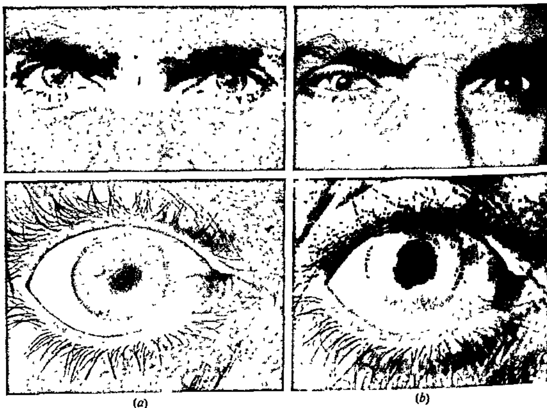
The advantage of this method is that a successful graft is likely to be crystal-clear, but since the eyeball must be opened complications are more numerous. It is a method which is applicable to dense scars involving the whole thickness of the cornea (Fig. 136*a*)

Partial thickness

For this method the scar should not involve the whole thickness of the cornea. Such a scar can be removed without opening the eyeball and can be replaced by a thin graft which is sometimes called a lamellar corneal graft. Although this method is generally free from serious complications it does not give the best visual results if the corneal scar extends to any depth. On the other hand, such a graft can be repeated on the same eye and it is ideal for therapy such as the application of a graft to an indolent corneal ulcer in the same way that a crossleg flap is used to treat stubborn varicose ulceration (Figs. 135*b*, 137*a*)

Combined (flange type) graft

The combined graft is a new method which is a combination of the two previous methods. The graft consists of a central portion of full-thickness and a partial-thickness collar (Figs. 138, 139). The whole graft is in one piece and has been referred to as a "mushroom graft" by Franceschetti and a "flange graft" by the present author. This type of graft seeks to secure a rapid sealing of the anterior chamber by the flange so that the undesirable complications of the full-thickness method, such as iris adhesion



(a) (b)

Fig. 136.—Full-thickness graft.

and leak, are avoided In the flange method additional factors of safety are ensured by the pre-placement of intracorneal sutures before the globe is opened, and of simplicity by the use of few instruments (Figs. 135, 138).

INDICATIONS FOR KERATOPLASTY

Corneal grafts are used for the following purposes: (*a*) to replace a portion of scarred cornea with a clear graft of homoplastic corneal tissue, thereby to improve vision. This is the "optical" graft. It may be of partial thickness or full thickness, or of the flange type; (*b*) to replace inflamed or degenerate tissue in order to promote rapid healing and not primarily for restoration of vision—this is the "therapeutic" graft and is comparable to the skin graft on an indolent leg ulcer; (*c*) to prepare an extensive and irregular corneal scar for a future optical graft—such "preparatory" grafts are of the lamellar type and are used where the host cornea is of irregular thickness; and (*d*) to improve the appearance of a sightless eye disfigured by staring, white, corneal scars. Cosmetic grafts of this type are lamellar and are often combined with platinum black tattoo.

SELECTION OF CASES

Density of scar

Corneal scars vary in their suitability for graft surgery. The thin scar of the dendritic ulcer situated in the central area of the cornea can be replaced by a partial-thickness graft with marked improvement of vision, whereas the dense scar of severe petrol burns or the vascularized scars of ocular pemphigus are likely to give little satisfaction. In general the more dense the scar, the less likelihood is the possibility of improvement by a corneal graft.



(a) (b)

Fig. 137.—Partial-thickness graft (lamellar graft).



(a) (b)

Fig. 138.—Combined (flange type) graft.

Age is no bar to operation, but extreme youth presents nursing difficulties. To obtain the best results the cause of blindness should be entirely corneal with no intra-ocular complications such as cataract, glaucoma or retinal disease. The scar should be moderately dense and should not include the whole extent of the cornea, for it is a well-known fact that if a graft can be inserted adjacent to a clear area of host cornea the chances of a permanent success are better than if it is placed like an island in a sea of dense scar tissue.

Prognostic considerations

The following diseases have been enumerated by Franceschetti in their degrees of suitability for operation.

Good prognosis.—Keratoconus, familial dystrophies, central corneal opacities and mild scars of interstitial keratitis.

combined with adrenaline 1/1,000. Regional orbital block is produced by retrobulbar injection of 1 per cent Xylocaine combined with 5–10 per cent alcohol; the alcohol prolongs the effect of the anaesthesia. The facial muscles are temporarily paralysed by a similar injection of the trunk of the facial nerve behind the neck of the mandible (O'Brien) or at the margin of the orbit (van Lindt). The operation of corneal grafting should be entirely painless apart from needle pricks.

Preliminary medication of an adult is by phenobarbitone, 3 grains, given one hour before operation or by Omnopon, ⅓ grain, given 15 minutes before operation. If general anaesthesia is preferred thiopentone with gas and oxygen has been the method of choice.

Full-thickness method

Since the eyeball is to be opened it is essential that there should be no pressure on the globe, and the ordinary lid speculum is therefore not employed as its weight would

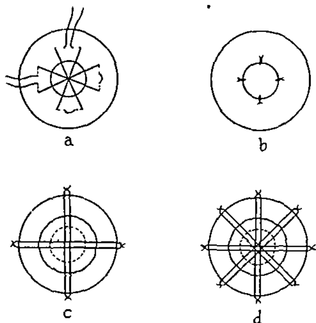


FIG. 140—(*a*) Overlay sutures (Tudor Thomas); (*b*) direct sutures (Barraquer); (*c*) overlay sutures with egg membrane (Paufique), (*d*) multiple overlay sutures with egg membrane (Rycroft).

tend to express the contents of the globe. Lid retraction is effected by sutures or by small clamps on the lid; movement of the eyeball is controlled by a traction stitch inserted through the superior rectus muscle. The first step in the operation is to mark the centre of the pupil on the host cornea with a spot of Bonney's blue ink. Since the pupil cannot usually be seen, on account of the scar, a point is marked slightly below and inwards of the centre of the cornea. The area of the scar is measured by calipers in order to determine the size of the graft required to cover the scar area. For full-thickness grafts this area should not exceed 6 millimetres, but for partial-thickness grafts it may be as much as 9 millimetres

Before the eyeball is opened two grafts are cut by punch from the donor eye. One is of the same size as the proposed graft and the other is 0.1 millimetre smaller. The grafts are placed in warm moist gauze until they are required; they should not be placed in saline as they would absorb fluid and swell. After the grafts are cut the next step is to insert retention sutures unless interrupted direct sutures are being used. These retention sutures cross from one side to the other of the cornea and are inserted with a 2-millimetre bite at the limbus; roughly, they conform to the pattern of the Union Jack (Fig. 140*d*). The sutures are then pulled aside ready for the preparation of the

graft bed. By the use of a Franceschetti trephine (Fig. 141) the bed for the graft is cut in the host cornea; great care is taken to proceed slowly, and experience will tell when the trephine has penetrated into the eyeball. If this step is performed too quickly the trephine will strike the anterior surface of the lens when the aqueous flows out of the eye and a traumatic cataract will be produced. Inspection must be carried out to ascertain that the edges of the graft bed are free from tags [illegible] is then [illegible] loop the [illegible] remain in position, and after a few minutes should be covered with a small circle of egg membrane which has been taken from the inside of a hard-boiled egg and cut to a diameter of 6–10 millimetres. The graft is thus protected from irritation of the overlay stitches and an immediate seal of the graft section is effected. When the egg membrane

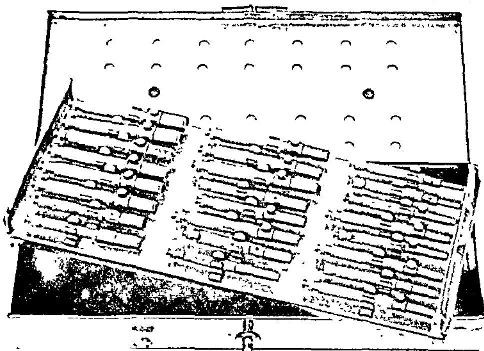


Fig. 141 —Box of Franceschetti trephines

is in position the graft sutures are brought over it and firmly tied, giving security to the graft. The upper lid which is flaccid and paralysed is brought down over the eye and a Paroleine pad applied. If interrupted sutures are used these are best applied by the use of 5–7-millimetre Grieshaber corneal needles and 00 braided black silk. They are passed through half the thickness of the graft and half the thickness of the host cornea; no stitch must penetrate the anterior chamber. About 6–8 sutures are employed for a 6-millimetre graft and they give great security of fixation. The disadvantage to the use of these sutures is that the graft has to be fixed and there is some trauma and separation of the lamellae at the edges. It is thought by some authorities that this separation predisposes to corneal oedema.

Partial-thickness method

In the partial-thickness method the graft bed is prepared by marking out the area with a suitable 7-millimetre trephine. A small angled knife is inserted at the

edge of the trephine mark and the cornea is split in one plane to facilitate the removal of a circular disc of scarred cornea without opening the eyeball; when this is removed details of the anterior chamber should clearly be seen through the base and no scar tissue should remain. A similar graft of partial thickness is cut from the donor cornea and placed into the graft bed, and then covered by egg membrane and sutures as described previously (Fig 142).



FIG 142 —Preparation of lamellar graft from donor eye

The flange graft

Franceschetti originated this method in 1950 and called it a "mushroom graft". In the flange graft the overlap is not as great as in the mushroom graft The object of this shape of graft is to obtain a rapid sealing of the section, thus to ensure an early restoration of the anterior chamber with less risk of iris inclusion in the wound. The first step in the author's method is to proceed as for a lamellar graft Sutures are then pre-placed in the graft and in the edges of the lamellar bed; the bed is 8 millimetres in diameter, in the centre of which a perforation is carried out of 6 millimetres. When this is completed the graft is pulled into place and the sutures securely tied Air is then blown into the anterior chamber to assist in keeping the iris and lens away from the section The air remains for about a week before it is absorbed.

POST-OPERATIVE TREATMENT

Both eyes are bandaged for one week and the patient is carefully controlled Retention of urine must be avoided and cough, if present, must be subdued. At the end of a week the first dressing is carried out under theatre conditions and the eye is inspected under cocaine anaesthesia. If all is well, retention sutures are removed and the graft should be held firmly in position with good apposition. There is generally some ciliary congestion but no undue discomfort or pain. Cortisone drops are commenced

10 days after operation and a careful observation is kept on the suture line to make certain that healing is not impeded by the cortisone; vascularization is generally much diminished and the eye quietens down. Estimation of vision may be carried out at the end of three weeks, but residual astigmatism may remain for as long as two months.

FACTORS WHICH INFLUENCE THE COURSE OF CORNEAL GRAFTS

Infection

The advent of antibiotics has practically eliminated immediate infection in cases of corneal-graft surgery. When infection does occur it is generally associated with conjunctival adhesions and burned lids with infected skin and deficient closure. Occasionally there is a late form of infection which occurs as a small residual abscess between the graft and its bed; this is probably due to aerial contamination at the time of operation. In the author's series of 80 lamellar grafts and 30 penetration grafts there was one case of residual infection and none of initial infection. One eye was lost three years after a successful graft through late infection brought about when damaged accidentally by a chrysanthemum stake. Scrupulous aseptic precautions are taken in the preliminary investigation of eyes which are to be grafted. Pre-operative control cultures and trial bandage cover are the rule. In this way infection has ceased to be a problem. Culture of the donor eye is also routine.

Technique

In no other form of grafting is technique so important, and it cannot be too strongly emphasized that corneal-graft operations should not be undertaken without the aid of such perfect eye instruments as are now available. It is a truism of graft surgery, as of cataract surgery, that an accurate section is half the operation and that every cutting edge of needle and trephine should be subject to slit-lamp scrutiny before operation. Just as the mechanical trephine of von Hippel in 1887 gave an impetus to graft surgery so the precise instruments which have been produced since World War II have profoundly influenced the course of corneal-graft surgery today; this is yet another problem which appears to have been solved.

Complications

The immediate complications of a graft operation include faulty apposition of the graft in the bed, uneven tension of the sutures causing distortion of the graft and a faulty section with loose tags.

Adhesion of the iris to the graft

More remote is adhesion of the iris to the graft section; if the adhesion is small it can be removed at a later date with little disturbance, but if the iris adheres on a broad edge then vascularization of the graft and secondary glaucoma will supervene. Glaucoma is always a menace of corneal grafts and will cause opacification of the graft if it is not controlled. Generally, the best form of control is by penetration cyclodiathermy or a fistulization operation.

Vascularization

Vascularization of the corneal graft is still a little obscure. The immediate super- [illegible] Secondly

third week resulting in a steady invasion of the graft by neovascularization followed

... alongside recent work in homo
... ible. Cortisone
... ularization, but
... ir faith to the
pplication of *beta* radiation of the host cornea before and after operation, but it is ifficult in these cases to have a control which would indicate the value of such idiation.

Oedema

Oedema of the graft is also a serious complication. In some cases it may be immediate nd the graft never really settles down In others it may be delayed until the third or



FIG 143—Host-donor junction Showing the junction of the graft and host after two years In the graft the absence of vessels and cells will be noted and the graft comes to resemble closely the appearances of the host cornea. (*a*) Descemet's membrane; (*b*) vascularized host cornea, (*c*) host-donor junction, (*d*) Bowman's membrane

fourth week, in which case it will come under the title of "maladie du greffon". There is some evidence to suggest that graft trauma during operation may predispose to oedema by causing separation of corneal lamellae.

The exact fate of the graft is not accurately known, but most experimental opinion inclines to the view that the graft is a scaffold graft in that the membranes of the original graft are retained but that the original cells are replaced by invasion cells from the host (Fig. 143).

RESULTS OF OPERATION

Opinions vary as to what constitutes a successful corneal graft. Some, like Tudor Thomas (1950), measure results by the clarity of the graft, arguing that the vision is not always a correct standard since there may be unpredictable disease of the posterior

10 days after operation and a careful observation is kept on the suture line to make certain that healing is not impeded by the cortisone; vascularization is generally much diminished and the eye quietens down. Estimation of vision may be carried out at the end of three weeks, but residual astigmatism may remain for as long as two months.

FACTORS WHICH INFLUENCE THE COURSE OF CORNEAL GRAFTS

Infection

The advent of antibiotics has practically eliminated immediate infection in cases of corneal-graft surgery. When infection does occur it is generally associated with conjunctival adhesions and burned lids with infected skin and deficient closure. Occasionally there is a late form of infection which occurs as a small residual abscess between the graft and its bed; this is probably due to aerial contamination at the time of operation. In the author's series of 80 lamellar grafts and 30 penetration grafts there was one case of residual infection and none of initial infection. One eye was lost three years after a successful graft through late infection brought about when damaged accidentally by a chrysanthemum stake. Scrupulous aseptic precautions are taken in the preliminary investigation of eyes which are to be grafted. Pre-operative control cultures and trial bandage cover are the rule. In this way infection has ceased to be a problem. Culture of the donor eye is also routine.

Technique

In no other form of grafting is technique so important, and it cannot be too [illegible] not be undertaken without [illegible] every cutting edge of needle and trephine should be subject to slit-lamp scrutiny before operation. Just as the mechanical trephine of von Hippel in 1887 gave an impetus to graft surgery so the precise instruments which have been produced since World War II have profoundly influenced the course of corneal-graft surgery today; this is yet another problem which appears to have been solved.

Complications

The immediate complications of a graft operation include faulty apposition of the graft in the bed, uneven tension of the sutures causing distortion of the graft and a faulty section with loose tags.

Adhesion of the iris to the graft

More remote is adhesion of the iris to the graft section; if the adhesion is small it can be removed at a later date with little disturbance, but if the iris adheres on a broad edge then vascularization of the graft and secondary glaucoma will supervene. Glaucoma is always a menace of corneal grafts and will cause opacification of the graft if it is not controlled. Generally, the best form of control is by penetration cyclodiathermy or a fistulization operation.

Vascularization

Vascularization of the corneal graft is still a little obscure. The immediate superficial vascularization is due to irritative trauma and is of no consequence. Secondly, there is the type which is an aggravation of existing deep vessels in an eye which is not quiet, but the serious type is the one which occurs towards the end of the second or third week resulting in a steady invasion of the graft by neovascularization followed

work in homo
ible. Cortisone
larization, but
ir faith to the
application of *beta* radiation of the host cornea before and after operation, but it is difficult in these cases to have a control which would indicate the value of such radiation.

Oedema

Oedema of the graft is also a serious complication. In some cases it may be immediate and the graft never really settles down. In others it may be delayed until the third or



FIG 143.—Host-donor junction Showing the junction of the graft and host after two years. In the graft the absence of vessels and cells will be noted and the graft comes to resemble closely the appearances of the host cornea. (*a*) Descemet's membrane; (*b*) vascularized host cornea, (*c*) host-donor junction, (*d*) Bowman's membrane.

fourth week, in which case it will come under the title of "maladie du greffon". There is some evidence to suggest that graft trauma during operation may predispose to oedema by causing separation of corneal lamellae.

The exact fate of the graft is not accurately known, but most experimental opinion inclines to the view that the graft is a scaffold graft in that the membranes of the original graft are retained but that the original cells are replaced by invasion cells from the host (Fig. 143).

RESULTS OF OPERATION

Opinions vary as to what constitutes a successful corneal graft. Some, like Tudor Thomas (1950), measure results by the clarity of the graft, arguing that the vision is not always a correct standard since there may be unpredictable disease of the posterior

TABLE I

Diseases	Patients	Grafts
Pemphigus of conjunctiva and cornea	3	4
Burns (a) Chemical	7	8
Burns (b) Thermal	3	3
Burns (c) Gas	1	1
Recurrent pterygium	1	2
Epithelial dystrophy of cornea	2	2
Band-shaped keratopathy	5	5
Acne rosacea keratitis	8	11
Disciform keratitis	1	1
Neurotrophic keratitis	1	3
Lipoidosis of cornea	4	7
Interstitial keratitis	3	2
Healed ulcers	8	9
Leucoma adherens	3	2
Active corneal ulcers	2	2
Total	52	62

Analysis of Results

The results obtained with the four different classes of graft are as follows:

Type of graft	No.	Improved	No change	Worse	Not Assessed
Optical	41	24	11	4	2
Therapeutic	9	6	3	—	—
Preparation	5	4	1	—	—
Cosmetic	7	7	—	—	—
Total	62	41	15	4	2

Optical grafts

Forty-one cases. The results of the optical grafts are classified according to visual improvement after operation by means of a fractional basis of percentage. Thus improvement of vision from perception of light to 6/5 represents 100 per cent, and each of the ten visual steps in between is equal to 10 per cent; for example, 6/60 to 6/24 represents two steps and is assessed as a 20 per cent improvement no matter where this occurs in the visual acuity scale. On this basis the 24 cases in which vision was improved by lamellar keratoplasty may be analysed thus

TABLE II

Stage of improvement	Degree of improvement (per cent)	No of cases
Perception of light to hand movements	10	7
Hand movements to counting fingers	20	5
Counting fingers to 6/60	30	2
6/60–6/36	40	4
6/36–6/24	50	5
6/24–6/18	60	—
6/18–6/12	70	1
6/12–6/9	80	—
6/9–6/6	90	—
6/6–6/5	100	—

In this series of lamellar optical grafts the longest period of donor-graft preservation was 21 days, in a case where vision was improved from hand movements to 6/36. No direct relationship in the post-operative reaction of the graft to the length of the period of preservation was established. The best visual result was obtained in a case of acne keratitis where vision was improved from perception of light to 6/9.

THE DONOR PROBLEM

It will be apparent that the expansion of corneal-graft surgery in Great Britain now mainly depends on an adequate donor supply. In the past there have been difficulties of infection, the lack of special instruments, the impact of two wars on the training of ophthalmic surgeons and the uncertainties of technique.

It may be said that these difficulties have now been resolved, but the provision of an adequate donor supply still remains. Up to 1922 the homoplastic corneal graft was usually taken from a freshly excised eye, and excision of eyes was much more common in the early part of this century than it is today. In the latter half of the nineteenth century and in the early part of the present century up to the present day the main source of donors came from fresh eyes which had to be excised either for injury or some disease of the posterior eye such as sarcoma. This source is diminishing as ocular surgery becomes more conservative and as infection is controlled; the use of radon and radium in the treatment of choroidal sarcoma is an example. In 1922 Filatov employed the cadaver eye after preservation in an ice chest, and it is obvious that this will have to be the main source of donor supplies in the future.

The best method of preservation has not yet been decided. Paufique favours saline vapour, Tudor Thomas uses saline or a moist chamber, Barraquer employs a dry test-tube on ice and Feldman uses partial dehydration as a means of preservation. At East Grinstead, Burki's method has been used by which the cornea is preserved in sterile liquid paraffin at 4° C. During that time the cornea is known to consume oxygen and Duane (1949) has reported that respiration is maintained in oil, but depressed to 70 per cent when the temperature drops to −40°. The viscosity of the liquid paraffin has been of special advantage in preventing damage to the eye during transportation. Such eyes have furnished successful optical grafts after three weeks' preservation, and the eye is suitable for preservation when it is removed from the cadaver within ten hours of death. Efforts have been made to provide an adequate donor supply of cadaver corneas by the Corneal Grafting Act of 1952. The immediate consequence of this alteration in the law has been the establishment of eye banks for the storage of eyes throughout Great Britain in appropriate centres where corneal-graft surgery may be practised, and with the co-operation of relatives, doctors and hospitals there is no doubt that a vast reservoir is available. It must be emphasized that this Bill is entirely voluntary in character and that no eyes may be removed without consent. The initial eye bank in Great Britain was founded by Tudor Thomas between World Wars I and II and it has been elaborated within recent years at the Corneo-Plastic Unit and Eye Bank at East Grinstead. It has been found in practice that the collection of bequeathed eyes works well. At East Grinstead a team is available to proceed immediately on notification of death, and it has always been found that relatives treat the occasion with a sense of dignity and duty and there has been no embarrassment.

The ideal donor graft is taken from an aged person who has died a natural death, and it should be obtained within ten hours of death; when preserved in sterile liquid paraffin at 4° C. such a cadaver eye will furnish grafts for as long as ten days of preservation.

CONCLUSIONS

It would appear that the difficulties of corneal-graft surgery which can be solved by surgical technique, such as perfection in operation-theatre work and instruments, or by administration such as donor collection, have been successfully overcome. Problems of oedema and vascularization lie within the confines of the laboratory, such as the parallelism in the immunological reactions of the skin as described by Medawar; it is probable that in this instance the operating theatre has outstripped the laboratory, and further improvement of results must await the conclusions of experimental research. In any event, owing to the delicacy of technique and the need for special equipment, the practice of the operation must remain limited to a few selected centres where proper facilities for bank storage exist and where trained personnel are available.

Ophthalmic surgeons who practise keratoplasty today would do well to glance back over their shoulders down the road of progress and note these milestones which have been passed. Names like von Hippel, Elschnig, Filatov, Tudor Thomas, Castroviejo, Franceschetti and Paufique clearly mark them, and their early efforts have now made it possible to restore the sight of many cases of corneal blindness for whom there was, hitherto, no hope.

ACKNOWLEDGEMENT

I wish to thank Mr. Gordon Clemetson, director of the Photographic Unit, Queen Victoria Hospital, East Grinstead, for his skilful photography.

(*See also British Surgical Practice* Cornea—Diseases and Injuries, Vol 3, page 165, S Key 104.)

BIBLIOGRAPHY

Dieffenbach, J. F. (1831). *v Ammon's Z Opht.*, 1, 172
Duane, T. D (1949) *Arch Ophth*, 41, 736.
Elschnig, A. (1930) *Arch Ophth*, 4, 165.
Feldman, P. B. (1844) *Arch Gen Med.*, May, 1.
Filatov, V. P. (1934) *Sov. W Ophthal*, B 34, Nr 2, S 222
[illegible]
Paufique, L, Sourdille, G. P., and Offrey, G (1949) *Les Greffes de la Cornee*
[illegible]
Zirm, E (1905). *Arch. Ophth.*, 64, 580.

In an attempt of a different kind to reduce endogenous androgen production, Trunnell and his associates (1951) administered progesterone or anhydrohydroxyprogesterone to 19 cases—9 previously untreated, and 10 in relapse following castration or treatment with oestrogen; while 8 of the former and 7 of the latter group showed improvement, the remainder were made appreciably worse. Of late, considerable doubt has come to be cast on the truth of the anti-androgenic mechanism, and Brendler, Chase and Scott (1950) in particular believe that further investigation of the role of androgens in prostatic cancer is required. That the endocrine control of carcinoma of the prostate is not simply a question of neutralization of androgen is also the opinion of Flocks and his associates (1951).

Stilboestrol.—In management, the serum acid phosphatase should be estimated before oestrogen is given (King and Delory, 1948; Oelbaum, 1949). If the level is raised, as when osseous and other metastases are present, its subsequent fall is an index of response and a guide to the correct maintenance dose. Stilboestrol is undoubtedly the synthetic oestrogen with which the greatest number of cases has been

a total of 20–30 milligrams daily, and in exceptional cases much more. An adequate maintenance dose is then assessed by the general and local condition, and by the level of serum acid phosphatase. It should not be less than 1 milligram three times daily, and may require to remain at 5 milligrams three times daily to minimize the risk of delayed activation. Riches (1949) suggests there is a tendency to give too small a maintenance dose, and does not believe that a higher dose involves any risk of earlier oestrogen resistance. It is of utmost importance that the oestrogen should be taken regularly and continuously for the remainder of life.

Results and side-effects

In favourable cases, improvement is usually prompt Symptomatic benefit is apparent in 80 per cent of cases, is maintained for over one year in 50 per cent, and most often consists in dramatic relief of metastatic or sciatic pain, with improvement in micturition and diminution of frequency. These effects are accompanied by softening of the prostate, disappearance of induration and nodularity, relief of compression effects, partial regression of secondary deposits and marked increase of appetite with gain in weight.

Side-effects may comprise testicular atrophy, impotence, gynaecomastia, and pigmentation of the nipples, areolae and mid-scrotal line. Less frequently, oedema and minor degrees of vasomotor instability are encountered. These changes should not be regarded as indications to stop treatment, but greater difficulty may be experienced with vertigo or nausea In such cases, stilboestrol may be replaced by other oestrogens such as dienoestrol (at similar dosage), ethinyloestradiol (0 1–0 5 milligram daily) or by longer-acting oestrogens such as triphenylchloroethylene or triphenylbromoethylene.

Secondary tumours

In connexion with a long-term sequel to oestrogen therapy in the male, namely, the development of cancer of the breast, Corbett and Abrams (1950) have described bilateral tumours of the breasts—almost certainly prostatic metastases—associated with prolonged stilboestrol therapy. More recently, [illegible]

legal implications in long-continued oestrogen therapy for whatever reason (*see* Medico-legal Abstracts, 1940).

Combined hormonal and surgical treatment

At an earlier stage it appeared that oestrogen treatment would produce therapeutic results equal to those brought about by castration, and was indeed to be preferred, the latter measure being reserved for those patients intolerant to oestrogens or those having relapsed under oestrogen therapy. Of late, however, more authors advocate orchidectomy combined with oestrogen therapy as the most effective treatment, and one giving better results than either measure alone (Harrison and Poutasse, 1951; Kimbrough and Rowe, 1951). This combination has also been used pre-operatively to increase the scope of curative surgical procedures. According to Flocks and his associates (1951), total prostatectomy should be considered in patients in whom the carcinoma is limited to the prostate, and who are under the age of 70 years. Again, in conformity with the above, castration should be a part of endocrine control in the majority of cases, although stilboestrol therapy may be reserved for later treatment when the patient begins to have evidence of pain and other deteriorative changes.

There is no question that the management of the reactivated local and metastatic lesions continues to be a major problem demanding further investigation of pituitary-adrenal factors (Harrison and Poutasse, 1951). Gahagan and Fischman (1949) who, in agreement with the above, believed that castration might in fact offer more than oestrogen therapy, also suggested x-irradiation of the adrenals as an additional measure. Meantime, the work of Huggins and Bergenstal (1951a, b and 1952), has shown that bilateral adrenalectomy, with maintenance on cortisone acetate, can indeed cause partial regression of advanced prostatic cancer in a proportion of cases —as also in a proportion of cases of mammary cancer. Only continued evaluation will show to what extent this constitutes a practical advance; it may be noted that adrenalectomy produces a variable degree of retardation in the growth of various transplantable tumours in the rat (Ingle and Baker, 1951).

Combined surgical, hormonal and radiological treatment

In a related connexion, Murphy and Schwippert (1951) believed pituitary irradiation to be of palliative value as an adjunct to orchidectomy and oestrogen treatment in prostatic carcinoma. In other cases—breast cancer and melanoma—Kelly and his associates (1951) found the tumours not to be affected and concluded that the adult pituitary is relatively resistant to x-irradiation in doses up to 10,000 roentgens. Shimkin and his associates (1952) found no definite effect of hypophysectomy on the progressive growth of a human melanoma, although unusual degenerative changes were found in metastases to the liver and spleen.

Cancer of the breast

Oestrogen therapy

[illegible]

of the breast (Cutler and his associates, 1949; Stoll, 1950; Paterson, 1950; Dargent and Papillon, 1951; Lewison and Chambers, 1952; for earlier references *see* Haddow, 1951). Unfortunately, the clinical response is highly unpredictable, although it now seems clear that beneficial responses are some three times more frequent in women over the age of 60 years than in those under that age, that oestrogens may, on the contrary, accelerate the course of mammary cancer in younger women, and that their therapeutic use should be restricted to cases 5 years or more beyond the menopause. Between 30 and 40 per cent of such cases may be expected to show subjective improvement; regression of local tumours, shrinkage and healing of ulcers, reduction in size of skin deposits and decrease in size of lymph node and pulmonary metastases. All

these responses are, however, temporary and rarely persist for more than a few months. Metrorrhagia may be a troublesome side-effect but is seldom severe. Although research continues, there is little real understanding of the mechanism by which the most striking regressions occur, knowledge of which would have great significance for the chemotherapy of cancer as a whole. In tracer studies of radioactive sodium oestrone sulphate, labelled with S^{35}, Lewison and his colleagues (1951) found that the concentration in mammary tumour tissue is notably higher than could be accounted for by random distribution throughout the body As for the oestrogen treatment of prostatic cancer, cases have been described of the coincident development of cancer in a fresh site in the course of protracted oestrogen therapy. Novak (1951) has described one such case of uterine adenocarcinoma in a patient receiving oestrogen, and the growth of circumstantial evidence certainly seems to suggest that oestrogens should be used with care in patients whose family history shows the slightest trace of predisposition

Androgen therapy

Androgen treatment is a further example of chemotherapy through alteration of the hormonal environment, and while in this case amelioration is perhaps more readily brought about in mammary cancer in women before the menopause, andro gens may be useful regardless of age. From the great volume of clinical investigation now available (Haddow, 1951; Preston, Taylor and Crumrine, 1949, Snelling, 1952) there has emerged a clear picture of the benefits to be expected. Subjectively these include a striking improvement in general health, increased sense of well-being, lessened pain and consequent diminution in the need for narcotics, and increased appetite and gain in weight. Objective changes mainly relate to the skeletal osteolytic metastases and are accompanied by evidence of recalcification or even hyperostosis, with elevation of the serum alkaline phosphatase and decline of the level of serum calcium in cases in which it was previously raised. Only a small proportion of cases can be expected to improve when there is local recurrence or distant spread, but administration of massive doses of testosterone may be followed by striking if temporary regression, as for instance of involved supraclavicular, cervical and axillary nodes, and of skin nodules, after total doses of the order of several grammes given over a few weeks· such regression may be accompanied by deposition of fibrous tissue and by cytological changes in the tumour cells. Great variation is to be expected in the speed with which the above effects become manifest thus, relief of pain may be evident within a week, while regressive changes may not be obvious for a month or more. Improvement in all cases is temporary only, although in many it may last for 6–12 months, and occasionally for several years, provided androgen treatment is not discontinued, instances in which patients have led useful lives for three years or more are by no means uncommon. But the benefit to be derived is always uncertain and unpredictable, and its duration difficult to forecast.

In management, testosterone, testosterone propionate, or methyl testosterone should be administered by the subcutaneous implantation of pellets or crystals, by intramuscular injection, or by the sublingual route, respectively. By intramuscular injection, 100–150 milligrams of testosterone propionate should be given thrice weekly for 8–10 weeks, or for longer periods if this can be achieved. A maintenance dose of 150 milligrams should be given weekly thereafter, or injection may be replaced by subcutaneous implantation. In this case the total dose should be 1,000 milligrams in the form of sterile fused pellets each of 100 milligrams implanted in the deep fascia of the anterior abdominal wall or over the scapula, and should be repeated in 4–6 months

Side-effects of androgen treatment.—The administration of androgens may be attended by oestrogen withdrawal effects, signs of masculinization, and metabolic

changes. The first may be observed within a month and consist of hot flushes and suppression of the menses. Signs of masculinization may become prominent in the later stages of treatment, but are by no means a necessary condition of its success. They consist of coarsening and increased sebaceous activity of the skin, acne, facial hirsuties and increased growth of hair on the limbs, with huskiness of the voice, enlargement of the clitoris and increased libido. The use of methyl androstenediol, a non-virilizing derivative of testosterone, has been suggested by Homburger, Kasdon and Fishman (1950), and by Foley (1950), in order to obviate these side-effects, and further reports are awaited. Other signs and symptoms, attributable to metabolic changes, are re-mineralization of the bones, and retention of water, electrolytes and nitrogen.

ENDOCRINE THERAPY OF TUMOURS OTHER THAN THOSE OF THE PROSTATE AND BREAST

Partial regression and other ameliorative effects are occasionally encountered following oestrogen treatment of tumours other than those of the prostate and breast. Thus palliation, including dissolution of papillomas and reduced vesical irritability as well as subjective relief has been recorded in cancer of the bladder (Lich and Grant, 1948), while other reports refer to disappearance of secondary deposits of malignant endothelioma in the lungs after administration of stilboestrol (Gunn Roberts, 1946), to temporary improvement in general condition and regression of metastases in lungs and vagina in a case of chorionepithelioma in which the dose of stilboestrol was gradually increased from 3 milligrams to 1,000 milligrams daily (Kullander, 1948), and to similar responses during hormonal therapy of malignant tumours of the nose and bucco-pharyngeal cavity. Lemon and his colleagues (1951) describe the administration of testosterone propionate (100 milligrams thrice weekly), as inducing nearly complete remission of the symptoms and signs of disease in a patient with osseous metastases from adenocarcinoma of the thyroid, and suggest its further trial in the palliation of thyroid cancer not responding to surgery or radiation. Regressive changes brought about by progesterone in carcinoma of the cervix were described by Hertz and his colleagues (1951), but were not regarded as sufficient to indicate the use of progesterone as a therapeutic agent. In leukaemia, Storti, Mauri and Mocchi (1951) found neither the development of the disease nor the ultimate result to be affected by oestrogens or testosterone.

HORMONAL TREATMENT OF HAEMOPOIETIC DISORDERS

Cortisone and ACTH in leukaemia and allied diseases

Many authors, including Pearson and his colleagues (1949, 1950, 1951), Farber and his colleagues (1951), Wintrobe (1950), Snelling and his colleagues (1951), Mickle and his colleagues (1951), and Schulman and his colleagues (1951), have reported on the use of ACTH and cortisone in acute leukaemia in both adults and children. On a dose of 25 milligrams of ACTH 6-hourly in adults, and about half this dose in children, approximately 50 per cent of cases may enter complete clinical and haematological remission. In these, chemical studies often indicate a mass destruction of leukaemic tissue. Great variation is observed from patient to patient, and also in the same patient, in regard to the cytological, physiological and biochemical effects of the hormones. The remaining cases do not respond, even to much increased dosage, and those undergoing remission inevitably relapse either during treatment or following it, the great majority proving unresponsive to subsequent therapy. Pearson and his colleagues (1950, 1951) have also studied the effect of ACTH on the chronic lymphomas, including chronic lymphatic leukaemia, lymphosarcoma, Hodgkin's disease, and related conditions. During the period of investigation there was rapid

regression of the lesions, but the underlying pathological conditions were not significantly changed, and the lesions rapidly returned when administration of ACTH was discontinued. In a study of 26 cases of advanced neoplastic disease treated with ACTH or cortisone, Taylor, Ayer and Morris (1950) observed only temporary regressions, while no significant alteration in the clinical picture or haematological findings was noted in 4 cases of lymphatic and myelogenous leukaemia treated with cortisone by Weder and Becker (1951): in the opinion of Mickle and his colleagues (1951), ACTH and cortisone are of less value than aminopterin in the treatment of acute leukaemia in children (*see also* below). Dameshek (1952) has furnished an interesting comment on a recent and somewhat pessimistic report by the Haematology Panel of the Medical Research Council: "In the acute and subacute leukaemia of infancy and childhood the steroid hormones induce a well-defined and even a complete remission in about 50–60 per cent of the cases. If ACTH or cortisone is given simultaneously with aminopterin a remission may be induced in almost every case. Although in most cases the remissions are not sustained for more than 2–4 months, in some cases excellent and even complete clinical and haematological remissions continue for a year or longer. In chronic lymphocytic leukaemia the steroid hormones are not infrequently useful . . " The difference of opinion is attributed largely to the dosage used: the cases referred to in the report received 1 gramme of ACTH and 1·5 grammes of cortisone over 10 days, whereas in Dameshek's opinion ACTH must be given in amounts of from 150 to 300 milligrams daily, and even this is sometimes ineffective.

THE NITROGEN MUSTARDS

Hodgkin's disease, the leukaemias and reticuloses

Recognition that the nitrogen analogues of mustard gas, or the so-called nitrogen mustards, can induce cytotoxic effects in a wide variety of tissues, and especially those in a state of active proliferation, originated from the study of these substances as potential agents of chemical warfare. The extensive literature, dealing with the cytological and pathological effects upon normal and neoplastic tissues, and the application of the mustards in treatment, has recently been summarized by Haddow (1951).

A remarkable feature of the mustards is the manner in which they reproduce many of the biological effects of high energy radiations, and the chemistry and biology of these and other "radiomimetic" substances have been discussed by Loveless (1950). Useful clinical responses are very largely confined to the spectrum of neoplastic disease involving the reticulo-endothelial system—the leukaemias, multiple myeloma, lymphosarcoma and reticulum-cell sarcoma, Hodgkin's disease, giant follicular lymphoblastoma, polycythaemia vera, mycosis fungoides, Boeck's sarcoid, and other but rarer allied conditions—although palliative effects have also been recorded in unrelated tumour types, and particularly carcinoma of the lung. The nature and extent of the response is preponderantly determined by the histogenesis of the tumour and by the inherent activity of any given compound, and McWhirter (1951) is correct when he doubts whether mere modification in the technique of administration of existing drugs is likely to increase their effect. Intensive experiment has also shown that it is by no means easy to enhance the biological activity of such compounds by chemical modification, although certain more recent members (*see* below), appear to exhibit potency of a degree not hitherto encountered, and may, after all, hold out some prospect of an advance in therapeutic efficiency.

Hodgkin's disease

In the treatment of Hodgkin's disease, many express the opinion that nitrogen mustard therapy should not be regarded as an adequate substitute for radiation,

but should be reserved for cases with marked constitutional symptoms and visceral involvement. In these, a period of marked rehabilitation may follow the use of one or several courses, although opinion is doubtful whether in fact the advent of the nitrogen mustards has seriously, if at all, modified the basic prognosis. Boland (1951) found little evidence of such and Gellhorn and Collins (1951) concluded from a study of 132 cases in equal groups receiving radiotherapy alone or radiotherapy plus nitrogen mustard in alternating courses, that nitrogen mustard, while a useful adjunct in the management of Hodgkin's disease, did not prolong life by its addition to conventional therapy. It may however be used with profit in cases for which radio-

alleviation may be marked, the chemical agent unfortunately offers no better prognosis, and the underlying pathology is unchanged (Block and Murphy, 1948). More encouraging results, with prompt haematological and clinical responses, are frequently although not invariably observed in polycythaemia vera (Spurr and his colleagues, 1950, Woodruff, 1948).

Bronchogenic carcinoma

Lynch, Ware and Gaensler (1950) described 60 cases of inoperable bronchogenic carcinoma treated with nitrogen mustard, of which 69 per cent showed moderate to excellent subjective relief, with objective evidence in 54 per cent. Objective improvement showed a relationship to tumour type, being noted in 83 per cent of undifferentiated types, in 50 per cent of squamous types, in 33 per cent of adenocarcinomas, and in only 11 per cent of epidermoid tumours. Roswit and Kaplan (1951) studied 40 cases of inoperable bronchogenic cancer which had received nitrogen mustard as a systemic adjunct when radiation appeared no longer feasible or effective: 30 patients experienced remission of severe subjective symptoms, while objective improvement was recorded in 19. From these and other papers, for example, Brown and Davis (1949), Benda and Aubin (1950), and Kent and Reh (1950), it appears that nitrogen mustard has a place in the palliative treatment of inoperable pulmonary cancer, especially in anaplastic types.

or

use

in the treatment of the chronic leukaemias. These drugs are administered intravenously as the hydrochlorides, in aqueous or saline solutions which should be freshly prepared, and should be given after an overnight fast, or late in the evening after a light diet and mild sedation. A white cell count should be taken daily during treatment, and a full blood count twice weekly. Dosage for HN2 is in the range of 0·1–0·2 milligram per kilogram of body-weight, on consecutive or alternate days, to a total of 3–6 doses, and is varied in individual cases according to the blood picture and to the response to previous doses or courses. The average total dose for a single

rather

0·1

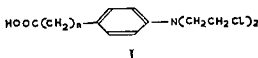
nd-

Side-effects of nitrogen mustard therapy

side-effects in nitrogen mustard therapy are nausea and vomiting,

produce more nausea than later ones, and the patient should be reassured beforehand.

As already indicated, much labour and ingenuity have been spent in an endeavour to produce variants of enhanced therapeutic efficiency, and several aromatic derivatives are now available which have one advantage in that they can be administered for long periods orally, and produce no acute side-effects. One of these, β-naphthyldi-2-chloroethylamine, has been extensively studied in clinical trial, at the Royal Cancer Hospital and elsewhere, but with relatively disappointing results (Matthews, 1950; Introzzi and Ninni, 1950; Nabarro, 1951; Galton, 1951), which indicate that it is less active than HN2, slower in action, and produces remissions which are less in frequency and extent, and are of shorter duration than those produced by the aliphatic nitrogen mustards: it may, however, be helpful in the treatment of polycythaemia vera (Iversen and Meulengracht, 1951). That the search for related compounds of



I

much higher activity may not be entirely fruitless is, however, shown by the more recent observation of exceptional potency in certain members of the series I, and particularly in that member in which n = 3. No indication of their clinical value is available as yet.

Triethylenemelamine

Apart from their clinical application, much attention has been paid in the past few years to the more fundamental aspects of the cytotoxic and cytostatic action of the nitrogen mustards. Thus, Haddow, Kon and Ross (1948), and others, have emphasized the correlation between biological activity and the presence in the molecule of a minimum of two reactive side-chains. On the basis of this and other evidence, Goldacre, Loveless and Ross (1949) suggested that the biological effects of these substances might primarily be due to a process of chemical cross-linkage between the constituent molecular chains of the chromosome fibre. While this view is now known to be unduly simple, and other possibilities are equally likely, it has led to the general conception of the action of these and similar agents by virtue of the alkylation of genetic protein In this way the hypothesis has provided a remarkable stimulus to the development of the subject, and, among other things, to the search for alkylating compounds of increased therapeutic efficiency—for example, various substances already utilized as cross-linking agents in the textile industry, among which many di-epoxides and polyethylene-imines have now been shown to possess cytotoxic action of the same general type as that already known in the case of the mustards.

The triethylenemelamine known as TEM (2 : 4 6-triethylene-imino-*s*-triazine, II) is of special interest in this connexion since it was originally devised by the Hoechst Farbwerke as a cross-linking agent of high efficiency and was later described by Lewis and Crossley (1950), and by Burchenal and others (1950a, b, c), as capable, with other ethylene-imine derivatives, of retarding the growth of various mouse leukaemias and other tumours. Its nitrogen mustard-like actions, and those of other bis(ethylene-imines) have been described by Philips and Thiersch (1950). The toxicity of this substance is about twice that of HN2, and therapeutic responses are obtained in the range of from 8 to 12 milligrams total dosage in the adult. Since TEM can be given intravenously without producing venous thrombosis or severe nausea or vomiting, and can also be administered by mouth, and is therapeutically as active as HN2, it has tended of late to supplant the latter in clinical practice By mouth, 5 milligrams is given with water on waking, breakfast being withheld for one hour. The single

tolerated daily dose is up to 10 milligrams, although this amount is the usual total given over 2–4 days. Subject to a white cell count twice weekly, the same course may be repeated at weekly or bi-weekly intervals, and in some cases a period of 4–8 weeks may be necessary to reach the therapeutically effective dose.

Rhoads and his colleagues (1950) have described how oral administration will induce temporary objective and subjective improvement in Hodgkin's disease and in chronic myelogenous and lymphatic leukaemia. The results are qualitatively similar to those produced by the intravenous injection of HN2, but nausea and vomiting may be avoided by the oral route and the agent may be particularly useful in the treatment of ambulatory patients. The indications are similar to those for HN2, and the slower and more prolonged action by oral administration may make it more useful. The toxic effects, which are identical with those of HN2, must, however, be very closely controlled to avoid serious depression of the marrow. In 43 cases, Bayrd and his colleagues (1951) found their results to be most favourable in chronic myelogenous leukaemia, less so in chronic lymphatic leukaemia, Hodgkin's disease,

II

Triethylenemelamine (TEM)

and lymphosarcoma. Meyer and his associates (1951) studied 17 adult cases of chronic leukaemia treated with TEM in doses of 10–125 milligrams over periods of 10–200 days, in courses ranging from 10 to 20 milligrams. Complete haematological and bone-marrow remissions occurred in 2 cases of chronic lymphatic leukaemia, but otherwise results were somewhat variable. Although in the hands of Paterson and Boland (1951) TEM appeared equal to established methods of treatment in cases of leukaemia, polycythaemia, Hodgkin's disease, and myelomatosis, these authors did not regard it as in any way superior. Shimkin and his colleagues (1951) point out that TEM has the disadvantage of a narrower chemotherapeutic range of dose (as compared with nitrogen mustard), and mention that the oral dose in lymphatic leukaemia, which is extremely sensitive, should not exceed 0·1 milligram per kilogram of body-weight. According to Hansen and Bichel (1951, 1952) depression of the bone-marrow occurs later than with nitrogen mustard, lasts longer [illegible] may sometimes be irreversible. In a series of 46 [illegible] kaemia, leu[illegible] and related diseases, Silverberg and Dameshek [illegible] the substanc[illegible] effective in generalized and radio-resistant ca[illegible] in's dis[illegible] occurring in 30 per cent and lasting as long [illegible] Cases of [illegible] and reticulum-cell sarcoma showed [illegible] while [illegible] ement was recorded in chronic [illegible] s [illegible] striking [illegible] splen[illegible] ly: complete rem[illegible] an [illegible] days, [illegible] a [illegible] e its maintena[illegible] 5 m [illegible] ined most [illegible] for long [illegible]

myelosuppressive action was regarded as making it valuable in the treatment of polycythaemia vera and thrombo-cythaemia. No benefit was obtained in acute leukaemia. In a series of 42 cases of neoplastic disease, Wright and his colleagues (1952) observed the most dramatic responses in cases of lymphosarcoma, Hodgkin's disease, and chronic myelogenous and lymphatic leukaemia, only moderate responses in fibrosarcoma, reticulum-cell sarcoma and mycosis fungoides, and none in cases of carcinoma.

1 : 4-DIMETHANESULPHONOXYBUTANE (MYLERAN) IN THE TREATMENT OF CHRONIC MYELOGENOUS LEUKAEMIA

Apart from the experimental test of substances already known to be capable of alkylating or cross-linking in other connexions, some success has already attended the development of bifunctional agents likely to possess such properties. Following the detection of high tumour-inhibitory activity in various sulphonic acid esters experimentally (Haddow and Timmis, 1953), it was decided that the correlation between chemical constitution and activity could best be studied by utilizing a simple structure to carry the functional groups, and one which would be easily capable of modification in regular gradations. The series (III) was therefore synthesized, in which n = 2 to n = 10. Biological activity is at a peak where n = 4 or 5, and in the former case (1 . 4-dimethanesulphonoxybutane), the compound has a specially pronounced action on the granulocytes, which observation has led to its clinical trial in cases of chronic myelogenous leukaemia, to which its use would so far appear to be confined In the series studied, relief of symptoms, general improvement, regression of enlarged spleen, rise in haemoglobin level, and fall in the leucocyte count with improvement in the differential count, have occurred during therapy (Galton, 1953) Although it is



III

still too early to assess the long-term value of such treatment, the results so far obtained have on the whole been both useful and impressive. The drug is more selective than nitrogen mustard or the folic acid antagonists in its effect on myeloid cells, and may be somewhat safer in use many cases have received daily doses of 4 milligrams by mouth for several months. In such doses, although it depresses myelopoiesis, it has little effect upon the lymphocytes and platelets, and side-effects are absent. Larger doses, however, depress the platelet count and cause haemorrhagic symptoms, and there is a danger of causing an irreversible depression of the marrow which may not become obvious for 4–6 months These effects show the necessity for the most careful haemotological control. The drug is of no value in the treatment of acute myeloblastic, lymphoblastic or monocytic leukaemia, or in acute relapse of the chronic leukaemias. Nevertheless it is of interest, within its strictly limited application and in the most favourable cases (Fig 145), as having yielded substantially useful clinical results equal to or surpassing those provided by chemical agents in this or other forms of malignant disease.

URETHANE IN LEUKAEMIA AND ALLIED CONDITIONS

Following the experimental demonstration by Haddow and Sexton (1946) of characteristic alterations produced by urethane and certain other carbamates in the mitotic division of animal cells, and of a concomitant retardation of the growth of various

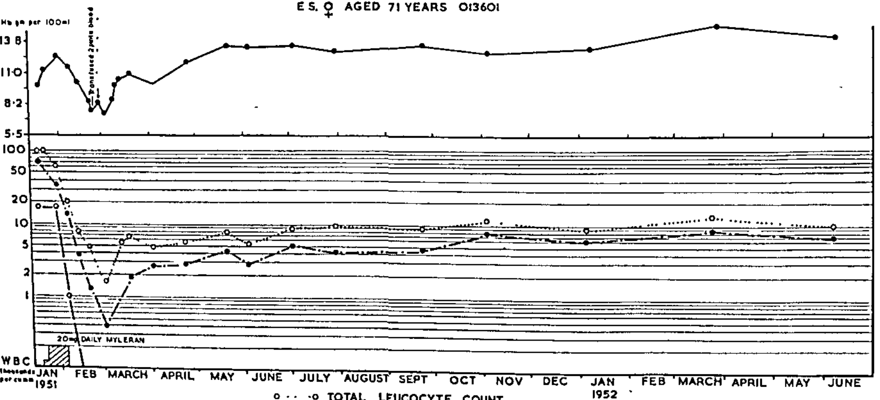


FIG. 145.—Unusually *favourable* response to the administration of Myleran in a case of chronic myeloid leukaemia.

transplantable tumours, clinical trial by Paterson and his colleagues (1946, 1947) revealed that urethane is capable of producing marked changes in leukaemia, such as a fall in the total leucocyte count to normal limits, an approach of the differential count towards a more normal pattern diminution in the size of the spleen and enlarged lymph nodes, and a rise in haemoglobin level. Although these effects are in general similar to those brought about by x-ray therapy, relapses take place and all the changes are essentially reversible. While urethane has doubtless been useful in a limited sense, its main interest probably lies in the advance which would follow an understanding of its mechanism of action: this is still obscure, but much has been contributed by Skipper and his school employing labelled compounds (1950, 1952), and especially the suggestion that urethane may inhibit the incorporation of formate in nucleic acid synthesis.

The most useful responses are met with in chronic myeloid leukaemia, in which some two-thirds of cases may show improvement and about half obtain remissions of about 2–6 months. In favourable cases the reduction in white cell count is accompanied by a rise in haemoglobin, the differential count approaches normal, and myeloblasts disappear. These changes are accompanied by an increase in red cells, the extent of which is important in assessing prognosis. Great variation may be observed in the time required for the blood picture to become more normal, for example, from a few days to two months or more, with total doses ranging from a few grammes to 200 grammes or more. In a most excellent and comprehensive account of the treatment of leukaemia as a whole, Whitby (1951) gives it as his experience that urethane has shown the best results in chronic myelogenous leukaemia and, save for a few cases of intolerance and failure, is as effective and less misery-making than x-ray irradiation It is, however, almost certain that urethane in this condition has now been superseded by Myleran, especially in view of the longer remissions which may be achieved by the latter substance, and the fact that these are not infrequently maintained for considerable periods even when the drug is withdrawn.

Although in chronic lymphatic leukaemia the effects of urethane are generally similar, only about 1 in 6 cases gives responses as satisfactory as those obtained in a much greater proportion of the myelogenous form. Decline in the white cell count, and diminution in the size of the spleen and of enlarged lymph nodes, is much less constant, and any rise in haemoglobin level does not bear the clear relation to prognosis which is seen in the myelogenous form. Since so much less benefit is to be expected from the use of urethane in chronic lymphatic leukaemia as compared with chronic myeloid leukaemia, radiotherapy, the nitrogen mustards, and agents such as triethylene malamine are to be preferred in most cases. No useful responses are to be anticipated in aleukaemic, terminal or acute leukaemias.

Administration

Urethane is usually administered orally, 1 gramme thrice daily in enteric-coated capsules being the dose most commonly employed, although smaller doses (for example 0 5 gramme 3–4 times daily) may be used to avoid nausea and produce a more gradual improvement, which can then be followed by a maintenance dose of 0·5–1·0 gramme daily. Administration by intramuscular or intravenous injection, or by rectal infusion, has little [illegible] , which [illegible] 40 per [illegible] therapy 1–2 grammes of urethane are dissolved in 20 millilitres of sterile normal saline solution, mixed with 200 millilitres of sterile normal saline, and administered over a period of 15–30 minutes

Side-effects

Of the side-effects produced by urethane, nausea is the most frequent, while drowsiness, giddiness and gastro-intestinal irritation are also encountered. More serious are the effects produced by excessive action of urethane upon the bone-marrow and liver: thus Meacham, Tillotson and Heinle (1952) have reported liver damage after prolonged urethane therapy, and Ohler, Houghton and Moloney (1950) a case of hepatic necrosis so caused.

Treatment of multiple myeloma

Among other conditions which may be favourably influenced by urethane, multiple myeloma is specially prominent and has been made the subject of an interesting study by Rundles and Reeves (1950), who appear to regard the action of urethane in this condition as representing an encouraging advance in practical therapy. In a later paper, Rundles, Dillon and Dillon (1950) describe how, as plasma cell growth is inhibited by urethane, abnormal serum components are reduced or may virtually disappear. These authors also mention an observation made in a case in which benefit from 10 months' continuous urethane therapy was followed by relapse, and which may be of much fundamental importance. When urethane was discontinued, the plasma cells in the marrow again decreased and proteinuria diminished, a phenomenon which these authors interpret as indicating that the prolonged exposure to urethane had rendered the plasma cells nutritionally dependent, so that their growth was once again inhibited by the drug's withdrawal. Harrington and Moloney (1950) also report a number of cases of multiple myeloma treated with urethane, of which a proportion showed relief of pain, gain in weight, improvement in anaemia, reduction in abnormal serum proteins, suppression of plasma cell proliferation and probable prolongation of life. A further series, of 66 cases with pathologically proved multiple myeloma treated with urethane over a 2½-year period, is provided by Luttgens and Bayrd (1951) Again there is some overall suggestion of prolongation of life. However, only 50 per cent showed subjective improvement, and only 20 per cent objective improvement. While their results appear not as favourable as in other series, these authors believe the administration of urethane to be probably as good a treatment as is available for multiple myeloma at the present time.

ANTAGONISTS OF FOLIC ACID AND OF THE "CITROVORUM" FACTOR, IN THE TREATMENT OF ACUTE LEUKAEMIA

As for many other agents in cancer chemotherapy (for example urethane), interest in the so-called folic acid antagonists is divided between the fundamental problem of their mode of action on the one hand, and their practical application on the other. In relation to the first, two vital steps were taken when Sauberlich (1949) discovered that the *Leuconostoc citrovorum* factor is capable of reversing the effects of aminopterin, and when the factor was identified and synthesized by Brockman and his colleag[illegible] factor was also stu[illegible] 950), Greens[illegible] among others, [illegible] the enzymatic conversion of folic acid to the citrovorum [illegible] the [illegible] of the citrovorum factor itself. The inter-[illegible] factor, with the purines and pyri-[illegible] ds, has been briefly considered by Girdwood (1952) [illegible] plastic anaemias, and from other work (for example Skipper, Morgan and Bennett, 1952) again it would appear that

the folic acid antagonists may conceivably operate through an inhibition of nucleotide synthesis.

The practical application of these agents has been fully considered by Warren (1952), as also by Dresner and White (1952). From a great number of papers (Farber, 1949; Dacie and his colleagues, 1950, Sacks, Bradford and Schoenbach, 1950; Meyer and Newman, 1951; Meyer and Rutzky, 1951; Burchenal and his colleagues, 1951; Jersild and Mehlsen, 1951), the results of therapy with aminopterin and its analogues such as amethopterin and aminoanfol appear to fall into three classes—no response, temporary clinical improvement, and (in the smallest number) remarkable and complete remissions which usually last for a short period only, but may on occasion be prolonged. Thus the most favourable results so far achieved in the treatment of acute lymphatic leukaemia and stem cell leukaemia in childhood have been obtained with aminopterin and related compounds, in the shape of remissions lasting over a year. Even though administration of these drugs is as a rule limited by the early development of toxic effects which render impossible their use over prolonged periods, it is remarkable that remission can be induced at all in such conditions. Hence there is no doubting the fundamental importance of these observations, the pursuit of which should lead to further progress.

The dose of aminopterin usually employed is 1 milligram daily, by intramuscular injection or orally, and of amethopterin, 2–5 milligrams daily.

THE CLINICAL USE OF RADIOACTIVE ISOTOPES

While the use of radioactive isotopes in treatment constitutes an extension of radiotherapy rather than a development of chemotherapy strictly, the topic is a closely neighbouring one and is included for the sake of completeness. On the place of isotopes in therapy generally, useful accounts have been given by Low-Beer (1950), Brues (1950) and Mitchell (1951), the last including reference to the treatment of polycythaemia with radiophosphorus and of thyroid carcinoma with radioiodine, and to the applications of radiosodium and radiogold. So far as concerns the treatment of metastatic thyroid carcinoma with radioactive iodine, the proportion of tumours concentrating the radio-element sufficiently for effective treatment appears to be disappointingly small. There are, however, reports of individual cases treated with remarkable success, as for example that of Walton (1950), in which an excellent response was induced in a girl aged 20 years with a fixed thyroid mass, involved lymph nodes in the neck and multiple secondary deposits throughout both lungs. Other individual cases are also of much interest, as for instance that of Bayrd and Hall (1948), describing an unusual remission after radiophosphorus therapy in a case of acute plasma-cell leukaemia. From the experience of Lawrence, Low-Beer and Carpender (1949) it appears that radiophosphorus therapy in their series of cases of chronic lymphatic leukaemia has been able to extend the span of comfortable life more effectively than other methods: 33 per cent had lived 5 years or more after the onset and 10 per cent for 8 years or more.

For chronic myelogenous leukaemia, Diamond and Craver (1951) describe 77 cases treated with radiophosphorus, with radiophosphorus plus x-ray irradiation, or with radiophosphorus and other chemotherapeutic agents, over a 10-year period, and, in agreement with others, believe that comfortable and useful life has been prolonged. The evaluation of radiophosphorus in primary polycythaemia, and in multiple myeloma, has been dealt with by Stroebel, Hall and Pease (1951) and by Lindgren, Bergstrom and Wihman (1951) respectively.

In an interesting account of the therapeutic potentialities of the radioisotopes, Brucer (1952) states that there are some 70 radioisotopes with half-lives between 12

hours and 60 days which might be produced in sufficient amount for therapy. At the moment, the number is some 25, while contamination with long-lived activities and competing reactions still further reduces the list in practice. While it is more than doubtful if the radioisotopes can furnish any permanent solution of cancer treatment, an immense amount of research is still required, much of which will be concerned with drug metabolism rather than with radiation itself.

(*See also British Surgical Practice:* Chemotherapy, Vol. 3, page 40, S. Key 90)

REFERENCES

Bayrd, E D, and Hall, B. E. (1948). *Blood*, 3, 1019
— Stickney, J M., Hall, B. E, and Watkins, C. H. (1951). *J. Lab. Clin. Med*, 38, 785.
Benda, R, and Aubin, H. (1950). *Bull. Soc. Méd. Hôp. Paris*, 66, 1376
Bichel, J. (1951) *Acta Radiol*, 36, 437.
Block, M, and Murphy, J. C. (1948) *Arch Path.*, 46, 519
Boland, J (1951). *Brit. J. Radiol.*, 24, 513
Brendler, H., Chase, W. E, and Scott, W. W. (1950). *Arch. Surg.*, 61, 433.
Brockman, J A., Roth, B., Broquist, H P., Hultquist, M. E., Smith, J. M., Fahrenbach, M. J, Cosulich, D. B, Parker, R. P., Stokstad, E. L. R., and Jukes, T. H. (1950) *J. Amer Chem Soc.*, 72, 4325.
Brown, A, and Davis, L. J (1949). *Glasg. med. J.*, 30, 197.
Brucer, M. (1952). *Merck Report*, Vol 61, 9.
Brues, A. M. (1950) *Amer. J. Obstet. Gynec*, 60, 1009.
Burchenal, J H (1950a). *Med. Ann Dist. Columbia*, 19, 17.
— (1950b) *Blood*, 5, 792.
— Crossley, M L, Stock, C. C., and Rhoads, C. P. (1950c). *Arch. Biochem*, 26, 321.
[illegible] Escher,
[illegible]
Erf, L. A. (1950). *Penn. med. J*, 53, 1172
Farber, S. (1949) *Blood*, 4, 160.
[illegible] King, J. P., and Ferrozi,
[illegible] *Urol.*, 66, 393.
[illegible]
Gardikas, C., and Wilkinson, J F (1952). *Lancet*, 2, 161.
Gellhorn, A, and Collins, V P. (1951). *Ann intern. Med*, 35, 1250.
[illegible] *ature*, 163, 667.
[illegible] *ph.*, 60, 181.
[illegible] 11.
[illegible]). *Cancer*, 4, 619.
[illegible] *e*, 167, 824
[illegible] 7(3), 469.
[illegible] 53.
[illegible] 11, 55.

Hertz, R , Cromer, J. K., Young, J .P., and Westfall, B. B (1951). *J Nat. Cancer Inst.*, **11**, 867.
Homburger, F , Kasdon, S C., and Fishman, W. H. (1950). *Proc. Soc. exp. Biol*, **74**, 162.
Huggins, C , and Bergenstal, D. M. (1951a). *J. Amer. med Ass*, **147**, 101.
— — (1951b). *Science*, **114**, 482
— — (1952) *Cancer Res.*, **12**, 134.
Ingle, D. J., and Baker, B. L. (1951). *Endocrinology*, 48, 313.
Introzzi, P , and Ninni, M. (1950). *Haematologica*, 34, 925.
Iversen, K , and Meulengracht, E. (1951). *Brit med. J*, **2**, 510.
Jersild, T., and Mehlsen, S (1951). *Acta Pediatrica*, 40, 127.
Karnofsky, D. A (1951) *Merck Report*, Vol 60, 4
Kelly, K. H., Feldsted, E. T., Brown, R. F., Ortega, P., Bierman, H R., Low-Beer, B. V. A., and Shimkin, M. B (1951). *J Nat. Cancer Inst*, **11**, 967.
Kent, L , and Reh, E P (1950). *Dis. Chest*, **17**, 190.
Kimbrough, J C., and Rowe, R. B. (1951). *J. Urol*, 66, 373
King, E. J , and Delory, G E. (1948) *Post-grad med J*, **24**, 299
Kullander, S (1948). *Lancet*, **1**, 944.
Lawrence, J. H., Low-Beer, B V. A., and Carpender, J W J. (1949). *J. Amer. med. Ass.*, **140**, 585.
Lemon, H. M., Ravin, I S , Ross, J F , Sisson, J. H , Anglem, T. J , and Branca, A W. (1951) *Cancer*, **4**, 1176
Lewis, M. A., and Crossley, M. L (1950). *Arch. Biochem* , **26**, 319
Lewison, E F , and Chambers, R. G. (1952) *New Engl J. Med*, **246**, 1
— Levi, J E., Jones, G. S., Jones, H W , and Silberstein, H E. (1951). *Cancer*, **4**, 537.
Lich, R., and Grant, O (1948) *J Urol.*, **59**, 682
Lindgren, E., Bergstrom, I , and Wihman, G. (1951) *Acta Radiol*, 36, 49
Loveless, A. (1950) *Nature*, **167**, 338
Low-Beer, B. V. A. (1950) *The Clinical Use of Radioactive Isotopes* Oxford
Luttgens, W. F , and Bayrd, E. D. (1951). *J Amer med Ass.*, **147**, 824
Lynch, J P , Ware, P. F , and Gaensler, E A. (1950) *Surgery*, **27**, 368.
McWhirter, R (1951). *Brit. J. Radiol*, **24**, 503
Matthews, W. B (1950). *Lancet*, **1**, 896
Meacham, G. C., Tillotson, F. W., and Heinle, R W (1952). *Amer J Clin Path*, **22**, 22.
Medico-legal Abstracts (1940)
Meyer, L. M., and Newman, A. (1951). *Amer J Med*, **10**, 452
— and Rutzky, J. (1951) *Cancer*, **4**, 1043
— Sawitsky, A., Beyers, M R., Ritz, N D , and Brahin, C. (1951) *Fed. Proc*, **10**, 324.
Mickle, K. G , Muscato, G. V., Lemanski, A., and Claudon, D B (1951) *J Paediatrics*, 39, 442.
Mitchell, J. S. (1951). *Brit. med J*, **2**, 747.
Murphy, W. T., and Schwippert, H. (1951) *Radiology*, **56**, 376.
Nabarro, J D. N. (1951) *Brit J Radiol*, **24**, 507.
Novak, E R (1951) *Amer J. Obstet Gynec*, **62**, 688
Oelbaum, M. H. (1949) *Lancet*, **2**, 912
Ohler, R. L., Houghton, J. D , and Moloney, W C. (1950) *New Engl J Med*, **243**, 984.
Paterson, E (1950). *Practitioner*, **165**, 488
— ApThomas, I , Haddow, A , and Watkinson, J M (1946) *Lancet*, **1**, 677
— — — — (1947). In *Approaches to Tumor Chemotherapy* Washington, Amer. Assoc. Advanc. Science.
— and Boland, J. (1951). *Brit J Cancer*, **5**, 28

..mer Phys ,
63, 136

[illegible]
[illegible] C. (1952) *J. clin. Endocrinol*, 12, 439.
Silverberg, J. H , and Dameshek, W. (1952) *J. Amer. med. Ass* , 148, 1015.
Skipper, H E (1950). *Tex Rep. Biol. Med.*, 8, 543.
— (1952) *Cancer Chemotherapy and Studies on the Mechanism of Action of Anti-Cancer Agents.* Progress Report of the Southern Research Institute, Birmingham, Alabama: August 15th, 1952.
— Morgan, C., and Bennett, L. L. (1952). *Cancer Res* , 12, 413.
Snelling, C. E., Donohue, W. L., Laski, B , and Jackson, S. H. (1951). *Pediatrics*, 8, 22
Snelling, M. D. (1952). *Arch. Middlesex Hosp.*, 2, 32.
Spurr, C. L , Smith, T. R., Bloch, M , and Jacobson, L. O. (1950). *J. Lab. Clin. Med.*, 35, 252.
Stoll, V. A. (1950). *Proc R Soc. Med.*, 43, 875.
Storti, E., Mauri, C , and Mocchi, N. (1951) *Haematologica*, 35, 493.
Stroebel, C F., Hall, B E., and Pease, G. L. (1951) *J Amer. med. Ass.*, 146, 1301.
Taylor, S G , Ayer, J. P., and Morris, R. S (1950) *J Amer. med. Ass.*, 144, 1058.
Trunnell, J. B , Duffy, B. J., Marshall, V., Whitmore, W. F., and Woodard, H. Q. (1951). *J. clin. Endocrinol.*, 11, 663
Walton, R. J. (1950) *Brit J. Radiol.*, 23, 559
Warren, S. (1952). *Blood*, 7, 97
Weder, C , and Becker, A. (1951). *Canad. med. Ass. J.*, 64, 39.
Whitby, L. (1951). *Brit. med. J* , 2, 1573.
Wintrobe, M. (1950) *Blood*, 5, 785.
Woodruff, A. W (1948). *Brit. med J* , 2, 299.
Wright, J. C , Prigot, A , Wright, L. T., and Arons, I. (1952) *Arch. intern. Med.*, 89, 387.

ACTINOMYCOSIS

See also B.S P , Vol. 1, p 60, S. Key 8.

Facial and cervical

Treatment

Pulmonary

Treatment

Chloramphenicol—LITTMAN, FUSILLO and PAUL (1952) describe a case of pulmonary actinomycosis in which chloramphenicol therapy was employed The patient was a man, aged 46 years, with a history of dental extractions for pyorrhoea and abscesses of the gums Subsequently an empy[illegible]
contain *Actinomyces* [illegible]
750 milligrams every [illegible]
empyema cavity. The [illegible]
showed no abnormality in the right lung field. Chloramphenicol therapy was continued and a complete dental clearance was made Cultivation of scrapings from the extracted teeth [illegible]

phenicol. There was no evidence, however, that the treatment had produced any adverse haemopoietic change. Similarly, neither leucopenia nor anaemia developed in a patient with a bronchial cyst, who received 260 grammes of chloramphenicol during a period of 56 days.

Glahn, M (1952) *Acta chir scand*, 102, 433
Littman, M L., Fusillo, M H , and Paul, J S (1952). *J. Amer med. Ass.*, 148, 608.

ADRENAL GLANDS

See also B.S P , Vol 1, p. 94, S Key 12.

Hypofunction and hyperactivity

[illegible]

administration of adrenocortical extract in large doses or of deoxycorticosterone acetate and sodium chloride or of both; hypotension during anaesthesia was controlled best by giving

aqueous adrenocortical extract, sodium chloride and whole blood. Cases of suprarer apoplexy (Waterhouse-Friederichsen syndrome) may be associated with lesions requiri surgical intervention, and operative cure may become possible, in the future, throu hormonal therapy. (2) Adrenal cortical tumours.
hormonal tumours are extensive haemorrhage an
anaesthesia is the provision of safe and adequat
syndrome present no anaesthetic problem unless
Cushing's syndrome. (3) Adrenal tumours of medullary origin. Sympathogonioma and neur blastoma present the problems associated with massive intra-abdominal resections. Phae chromocytoma necessitates pre-anaesthetic correction of the hypersecretion of adrenaline arterenol (4) Bilateral adrenal extirpation is made possible by adequate hormonal replac ment, to control the surgically induced Addison's disease. The authors emphasize the nee for avoiding anaesthetic agents and techniques which are associated with the risk of anox or asphyxia.

Malignant tumours

Phaeochromocytoma

Adrenaline and nor-adrenaline effect on the benzodioxane test.—TULLOH (1952) describe

the literature and found 4 cases of phaeochromocytoma in which a similar result was ob

contains a large content of nor-adrenaline If the presence of a tumour is suspected, the tes should be repeated. X-ray examination of the abdomen is of value, but insufflation of perirenal air requires the supervision of an expert. In the author's case an operation was performed, but no tumour was discovered The patient died 5 weeks later, and necropsy revealed a large phaeochromocytoma of the right adrenal gland The tumour was deeply situated under the right lobe of the liver.

Comparison with pink disease.—NEILL and SMITH (1952) point out that chromaffin-cell tumours are rare in children and only 9 cases under the age of 13 years have been recorded. The authors report on a case of bilateral phaeochromocytoma in a boy aged 6 years, which was fatal, and in which there were peripheral vascular changes and arterial hypertension The rarity of the neoplasia and the problems of differentiation from pink disease (or juvenile acrodynia) make the case all the more important Several clinical features common to both phaeochromocytoma and acrodynia were found, including skin changes, sweating, tachycardia and arterial hypertension. On the other hand, the typical changes of acrodynia, such as profound misery and irritability, were not shown in the personality of the child The child's age

suggested that it may be of interest, in future cases of acrodynia, to look for evidence of adrenal medullary hyperactivity. Early laparotomy is recommended in view of the diagnostic difficulties

Neill, Catherine A , and Smith, Gwen (1952). *Arch Dis. Childh.*, 27, 286.
Papper, E M., and Cahill, G. F. (1952). *J Amer med Ass.*, 148, 174
Tulloh, H. P. (1952) *Brit med. J*, 1, 531

AFTER-CARE—POST-OPERATIVE

See also B S P., Vol I, p. 130, S. Key 17.

Pain prevention

an aqueous nature in order to minimize the tendency to encapsulation and necrotic tissue

the incision, or by intercostal, lateral or paravertebral block. The amount of Efocaine injected varied, from 1–2 millilitres in each space, in 8 cases of cholecystectomy, to 10–17 millilitres in 7 cases of hysterectomy The degree of control of post-operative pain which was obtained was excellent in 79 cases and good in 21 cases This was achieved even in cases in which much visceral manipulation had occurred A study was made of the post-operative drug requirements of patients injected with Efocaine, as compared with the histories of untreated control cases in the hospital records. The result showed that these requirements were virtually eliminated for the treated patients There was no instance in any of the treated cases of local or systemic reactions or of complications Administration of Efocaine made the convalescence of the patients much more pleasant, facilitated early ambulation, and effected a reduction in the amount of nursing care required

Iason, A. H, and Shaftel, H E (1952) *Amer J. Surg.*, **83**, 549

ANAESTHESIA

See also B S P., Vol 1, p 205, S Key 26

Preparation of patient

Relaxants

Abnormal sensitivity.—GRAY and DUNDEE (1951) describe 4 cases which showed hyper-

thenia gravis (a condition which is associated with hypersensitivity to competition-blocking agents), showed a normal response to decamethonium but was hypersensitive to *d*-tubo-

nephrectomy remained completely apnoeic for 2 hours after the administration of 15 milligrams of the new relaxant, Win 2747, and had intercostal paralysis for a further 40

given alternately to a man who was undergoing a partial gastrectomy. The degree of respiratory depression became less after each successive dose of 4 milligrams of decamethonium, whereas after *d*-tubocurarine the degree and duration of respiratory depression increased The authors point out that these cases demonstrate again the importance of administering a test dose of relaxant drugs

Gray, T C, and Dundee, J. W (1951) *Lancet*, **2**, 1015

ARTHRITIS—SURGICAL CONSIDERATIONS

See also B S P, Vol 1, p 371, S Key 38.

Osteoarthritis

the first carpo-metacarpal joints, the great toes and first tarso-metatarsal joints, the inter-

[illegible]

cystic swellings on the finger joints; these burst and discharge a glairy fluid. The pain may also be of a deep aching type. (2) After several months the acute phase subsides and the chronic phase ensues, this being characterized by massive bony outgrowths around the articular margins. There is little pain and, in spite of the deformities, the joint often retains a fair range of movement, and function is largely restored. There are not any constitutional disturbances but the erythrocyte sedimentation rate is often raised. Radiologically the changes consist in (1) narrowing of the joint space, (2) marked sclerosis of the subchrondal bone, and (3) florid bony outgrowths at the articular margins. The authors state that, apart from proper management, there is no specific treatment, oestrogen therapy being of no benefit.

Kellgren, J. H., and Moore, R. (1952). *Brit. med J.*, **1**, 181.

BLADDER—TUMOURS

See also B S P., Vol. 2, p. 140, S. Key 58.

Early diagnosis

[illegible] sis [illegible] on [illegible] on [illegible]

metastasis, whereas only 2 out of 61 patients with deeply invading tumours survived 5 years. Only 10 per cent of patients with superficially infiltrating tumours died with evidence of extension of the vesical cancer, as compared with 85 per cent of those with deep tumours [illegible] examination is performed [illegible] the [illegible] plete extirpation, in such cases, produces a 5-year survival rate of 74 per cent, compared with 3 per cent in cases with late or neglected symptoms, or in which early diagnosis is followed by inadequate treatment

Treatment

Total cystectomy for carcinoma

Results—The results of total cystectomy for carcinoma of the bladder are reviewed by Colby (1952). In a series of 116 cases the operative mortality was 20 cases. Out of 96 survivors, 66 have died since their operation; 40 of these are known to have died from cancer, and 16 died from uraemia, sepsis or pyelonephritis. Recurrences have been seen 5 years post-operatively A review has been made of the records of more than 700 patients treated [illegible] tissue

[illegible]

Colby, F. H (1952). *Canad med. Ass J.*, **66**, 144.
Jewett, H. J. (1952) *J. Amer. med. Ass.*, **148**, 187.

BLOOD AND BLOOD-FORMING ORGANS: BLOOD EXAMINATION

See also B.S.P., Vol. 2, p 159, S Key 60

Coagulation

[illegible] scribes observations on the role of coagulase- [illegible] with staphylo-coagulase) in blood coagulation. [illegible] -coagulase cannot clot purified fibrinogen, but

defect in haemophilia can be corrected *in vitro* and *in vivo* by supplying this coagulase-globulin fraction.

Prothrombin

Thrombin conversion; prothrombin determination—QUICK (1952) discusses prothrombin, which he defines as the mother substance of thrombin As a clotting factor, prothrombin

Blood volume and volume of erythrocytes

Effect of injection of dextran

MEYER and his co-workers (1952) describe the changes in blood volume occurring in 6 patients in good clinical condition and in 1 patient with cirrhosis of the liver, after the administration of 500 millilitres of 6 per cent dextran in normal saline solution with that in 3 controls who received 500 millilitres of normal saline solution under similar conditions Red blood cells were labelled with radioactive phosphorus (P^{32}), and blood volumes were

injection of normal saline solution without dextran

Meyer, L. M., Berlin, N I, Hyde, G M., Parsons, R. J, and Whittington, B. (1952). *Surg. Gynec. Obstet.*, 94, 712
Miale, J. B (1952). *Amer. J clin Path.*, 22, 218
Quick, A. J. (1952) *Amer. Practic Phila.*, 3, 397.

BLOOD TRANSFUSION—THEORY

See also B.S.P , Vol. 2, p. 210, S. Key 63.

Whole blood substitutes

Dextran

In burns and shock.—HETZEL (1952) has studied the clinical use of dextran as a plasma substitute The groups of cases investigated were as follows: (1) a preliminary group; (2)

... and peripheral circulation; urinary estimations of dextran were made, for periods of 3–6 days, in 3 cases After the shock had been relieved tests of liver f... centration were made in 6 c

effects of infusing dextran d... ing to normal as the serum-dextran level fell The renal function was not impaired, except in 2 patients in whom lower-nephron nephrosis developed. There were 2 patients who died during the treatment of shock; necropsy revealed no indication of pre-existent renal disease, but the findings on section were those of lower-nephron nephrosis in 1 case and sucrose nephrosis in the other. Tests of liver function showed no instance of special change The cases in the present series showed no evidence of toxicity, no febrile reaction, and no sensitization phenomena

Effect on blood typing and cross-matching—The effect of dextran on blood typing and

treatment requiring expansion of the blood volume.

Transfusion reactions

Prophylaxis

Prevention of post-operative anuria—The technique of transfusion in relation to the prevention of anuria is discussed by COLE (1952) The term, anuria, is used here to include oliguria. In a period of 12 months, 4 (or 5) cases of post-operative anuria were seen; the Abbott intravenous sets were used in transfusion It was observed that, when the last few drops of a bottle of blood ran in, the saline solution, to which the bottle of blood was connected, invariably became coloured throughout with blood. It is now the author's practice, before starting to give a second pint of blood in the operating room, to remove the blood-stained saline solution and substitute for it a fresh bottle, so that there is little or no mixture of

surgery in the author's hospital, in the future, will be cross-matched between donor and donor, as well as with the patient's own blood

Cole, F (1952) *Amer J. Surg*, 83, 92
Hetzel, P. S (1952). *Med J Aust.*, 1, 657
Roche, P., Jun , Dodelin, R A , and Bloom, W L. (1952). *Blood*, 7, 373

BONE—ACUTE AND CHRONIC INFECTIONS

See also B S.P., Vol. 2, p. 241, S. Key 66

Osteosclerosis

Melorheostosis of long bones

Aetiology, diagnosis and treatment—Melorheostosis, a rare form of osteosclerosis (in which ivory-like new bone is found in a linear track through the shaft of a long bone), is

considered by WALLENSTEN (1952). This condition has also been termed osteosis eburnisans monomelica and osteopathia hyperostotica congenita membri unius. The author describes a case which is the fifth reported from Scandinavia, and at the earliest age (3 years and 8

ing ribs. Various theories have been put forward as to the aetiology of the disease, but the most acceptable one to the author is that of Zimmer, who believes the disease to be caused by a lesion of the *anlage* bud of the extremity involved. The clinical features comprise a group of vague symptoms. Commonly the disease starts in childhood, and often it is distinguished by a low-grade deformity of a finger or toe, associated with mild pain in the limb affected,

static disturbances.

Osteomyelitis

Treatment

A case of sternal osteomyelitis in a male patient aged 26 years is reported on by VELLACOTT

begun; operation was performed the next day. Pus taken from the manubrium grew coagulase-positive *Staph. aureus*. Administration of penicillin was continued, and the patient had completely recovered a month later.

Osteomyelitis and chondritis

Sternal and costal infections

Treatment.—BROWN and TRENTON (1952) discuss the treatment of costal chondritis and

chondritis is probably secondary to infection of mediastinal lymphatic glands; involved glands can be seen at operation. Operative procedures are often inadequate. Proper management is facilitated by bacteriological studies, Lipiodol injection of sinuses, whenever feasible,

biotics, particularly streptomycin in tuberculous cases, provide an adjunct to operative treatment, but the authors have not found that these are a substitute for surgery. An account is given of 9 cases, of which 8 were probably tuberculous in origin, tuberculous mediastinal lymphatic glands having been demonstrated and excised at operation in several instances. A pyogenic infection, in 1 case, was secondary to drainage of a subdiaphragmatic abscess. Treatment produced healing in all cases.

Brown, R. B., and Trenton, J. (1952). *Ann. Surg.*, 135, 44
Vellacott, D. (1952). *Lancet*, 1, 749
Wallensten, S. (1952). *Acta chir. scand.*, 102, 463

BONES—ERRORS OF DEVELOPMENT AND GROWTH

See also B.S.P., Vol. 2, p. 258, S. Key 67.

Infantile hyperostosis

Symptoms

MATHESON and MARKHAM (1952) report on 2 cases of infantile cortical hyperostosis. Both the cases showed two of the three salient features of the condition, namely, (1) irritability and

cortical hyperostosis was made. After her admission to hospital as an in-patient, the infant's temperature rose to 100–101° F , and 8 days later diarrhoea and vomiting developed; 5 days later she died Case 2 had a normal temperature and pulse and respiration rates The only abnormal findings were swellings, overlying both mandibles, which were hard and non-

these cases, is an extreme irritability, possibly due to pain in the bones.

Matheson, W. J., and Markham, Mary (1952). *Brit. med. J.*, **1**, 742.

BONES—NEW GROWTHS

See also B.S.P., Vol. 2, p. 298, S. Key 69.

Osteoid osteoma, fibrous dysplasia, eosinophilic granuloma

Diagnosis and treatment of children

A review was made by Walker (19

logical and pathological findings wer

eventually to correlate the findings (

lesion but m
recorded case
often seen in
surgically or

Myeloma

Plasmocytoma

Progression to myelomatosis.—Dalgaard and Dalgaard (1952) report on 3 cases of

signated as cases of solitary
emotological and chemical
with typical signs of myelo-
and in great pain. In the
re found in all 3 cases. In
the presence of myeloma
ion or (3) an increase
the erythrocyte sedi-
manifest itself, how-

primary tumour, anaemia of the organs, hyperplasia of the bone marrow and, in 2 cases, visible myelomas in the skeletal system The microscopical appearances were uniform and were typical of malignant plasma-cell myeloma. The author acknowledges that the question as to whether or not multiple myelomatosis usually begins as a solitary myeloma or plasmocytoma, with subsequent metastasis through the bone-marrow system, cannot be solved on the basis of these 3 cases which, after lapses of 9 years, 4½ years and 6 months, respectively, passed from the stage of distinct solitary plasmocytomas into cases of myelomatosis.

Malignant osteoclastoma

Transition from benign neoplasm

Clinical picture, treatment and end-results.—A case of malignant osteoclastoma of the lower end of the femur is described by CAMERON and MARSDEN (1952). A male patient, aged 34 years had a large swelling of the right knee which had been present for over a year. It

was regarded as an osteoclastoma, although histological appearances were not precisely those of a benign osteoclastoma. It is pointed out that the short history, as well as absence of the usual predisposing causes, makes it improbable that this was a benign tumour which later became malignant

Treatment of radial tumour

Fibular transplantation —LAWSON (1952) has used a fibular transplant in the treatment of

operation. Although there was evidence of some contamination of the wound with tumour cells at operation, no recurrence has appeared so far

Cameron, J A P , and Marsden, A. T H. (1952) *J. Bone Jt Surg.*, 34B, 93
Dalgaa
Lawsor
Walker

BRAIN—ABSCESS

See also B S P , Vol. 2, p 323, S Key 71.

Treatment

Aspiration

Antibiotic replacement —Because proof of the existence of a brain abscess is difficult,

show that thrombosis of the lateral sinus often precedes formation of otogenic cerebellar abscesses, all of which he found near the temporal bone and in the antero-superior part of

cases penicillin greatly reduces oedema around an abscess, but rising pressure may jeopardize life before the optimal time for intervention is reached. Early aspiration should be tried and though it may fail, later attempts often succeed. It may be better to operate on the ear first, but since general anaesthesia may cause a fatal rise of pressure, aspiration of the abscess under local anaesthesia may be an essential preliminary. About 4 weeks are needed for the encapsulation of an abscess, but injection of Thorotrast accelerates the process and does not hinder the activity of penicillin. This has been given systemically and also locally, as have other antibiotics. In numerous cases, using suitable burr-holes, pus has been evacuated and abscesses have been cured by shrinkage and scarring

End-results —JOOMA, PENNYBACKER and TUTTON (1951) discuss the relative value of aspira-

27 per cent. The risk of neurological deficits was less with aspiration than with excision. The recurrence rate after aspiration or drainage was 8 per cent, but there was no recurrence

per cent of the patients who had post-operative fits; the incidence of this complication in cases of frontal-lobe abscess was considerably higher after aspiration or drainage than after excision; whether the abscess capsule was left in the brain or was primarily or secondarily excised made little difference It is considered that regular and indefinitely prolonged anti-convulsant therapy after operation is necessary and valuable, even when the fits were apparently controlled by phenobarbitone In one case, in which neither anti-convulsant treatment nor phenobarbitone was given, the first manifestation of epilepsy was fatal status epilepticus. The authors' findings slightly favour excision as the best method of treatment for brain abscess

Jooma, O V , Pennybacker, J. B , and Tutton, G K. (1951). *J. Neurol.*, 14, 308.
Wood, P. H (1952). *J. Laryng* , 66, 71

BRAIN—TUMOURS AND TECHNIQUE

See also B.S P , *Vol. 2, p 420, S. Key 76.*

Diagnosis and localization

...AVIS (1951) describes the use of radio-... ...acranial lesions. About 1·1 millicuries of the dye, contained in sterile 8–10 per cent solution, were injected intravenously. Then the uptake in the brain was determined by means of a differential radiation localizer, consisting of a Geiger-Muller tube fitted with a lead shield, a counting-rate meter and a ... at the surface of the head was found to be maxi-... ...rded within 2 hours.

...accurate results are ... vascular permeability

...ake of the dye, for these lesions are characterized ... and newly formed capillaries. Cystic tumours fail ... the dye to ... degree. In some cases, however, it may be possi... the presence ... tion by detecting an area of decreased ... Hy... may produce a similar ...

the suspected tumour, and the extent of the tumour was traced fairly accurately In the

Extradural haematoma

Differential diagnosis

LEMMEN and SCHNEIDER (1952) report on 3 cases of extradural haematoma involving the posterior fossa, which serve to illustrate the wide variety of clinical signs and symptoms en-

established and removal of the clot was carried out promptly It appears that, in cases of supratentorial lesions, the presence of the extradural lesion in the posterior fossa may not be early recognized because of the slow development of clinical manifestations. Furthermore, intracranial decompression by cerebrospinal-fluid otorrhea may minimize the signs of increasing intracranial pressure, so that the presence of an epidural haematoma of the posterior fossa may not be identified Some authors have suggested a diagnostic criterion for closed extradural cerebellar haematoma, and the general opinion is that, unless prompt surgical intervention with removal of the clot is performed, death may become imminent The

Meningioma

Aetiology

the development of the so-called melanoblastic and lipomatous growths It has been found

that the great variation in size of both meningiomas and arachnoid granulations make differentiation of a true tumour from a hypertrophied granulation impossible in some situations.

Medulloblastoma

Diagnosis, treatment and end-results

Quoting the calculation that about 16 per cent of all brain tumours occur in children under 15 years of age, SMITH (1952) describes 34 cases in which, since medulloblastoma is common, the outlook was poor. Most tumours in children are below the tentorium and those above are near the third ventricle Of the latter type, 11 are described. Diagnosis may rest on vomiting, unsteadiness and Macewen's sign, but, since the skull sutures separate easily, papilloedema may develop late Rapidly growing tumours are common; they tend to enlarge the head and to metastasize widely in the central nervous system, so that decompression and post-operative radiotherapy are usı

of the tumours in children may b·

respectively, and the tumours were, respectively, a fourth-ventricle medulloblastoma, an unclassified third-ventricle tumour, and a cerebral glioblastoma multiforme with much calcification.

Cysts

Posterior fossa dermoid cysts

Aetiology.—LOGUE and TILL (1952) discuss dermoid cysts of the posterior fossa, with special reference to intracranial infection. These cysts arise from misplacement of fragments of ectoderm in the vicinity of the developing neural tube at about the third or fourth week of

material and cholesterol,

, which, at operation,

may occur anywhere

a at or near the mid-

graphic appearances. Attention is drawn to the ease with which infection

and thus cause meningitis or an abscess and, in particular, to intradural dermoid cyst with a complete dermal sinus.

Belcher, E. H., Evans, H. D., and de Winter, J. G. (1952). *Brit. med. Bull.*, 8, 172.
Davis, L. (1951). *Ann. R. Coll Surg., Engl*, 9, 349.
J. Neurosurg., 9, 245.
1, 1.
70.

BREAST—CARCINOMA OF

See also B.S.P., Vol 2, p. 456, S. Key 77.

Treatment

TON (1952), the fact that the mammary

women, together with the increasing

therapy has been of some value when metastasis existed, but the results were unchanged when axillary involvement was not present.

Medical treatment

Sex hormones.—The recent increase in cancer, occurring independently of greater longevity, is emphasized by LEWISON and CHAMBERS (1952), who suggest that improvements in treatment may depend on methods not involving surgery. The authors treated 80 patients with advanced mammary cancer by androgens or oestrogens for at least three months Although the clinical response was unpredictable, some patients responding to one remedy and others to another, the authors conclude that valuable palliative results are obtainable It was noted that oestrogens were most valuable for women who had passed the climacteric. It did not appear that prior treatment with sex steroids affected the results, but, even in cases which were clinically hopeless, the subjective improvement was often, considered alone, a justification for their use. Since positive identification of cancer cells is often so difficult, it is considered probable that operations will continue to show a heavy mortality within 5 years When using testosterone, a weekly dose of 300 milligrams was found most suitable, and with this dosage 4

incipient cardiac failure were sometimes troublesome, while nausea and vomiting called for the exercise of patience. The authors regard sex-hormone treatment as holding out much hope for the future

Harrington, S W. (1952) *J. Amer. med Ass*, **148**, 1007
Lewison, E. F, and Chambers, R. G. (1952) *New. Engl. J Med*, **246**, 1.

BURNS AND SCALDS

See also B.S P, Vol. 2, p 518, S. Key 82.

Burns

Second-degree burns

Management of patient—EVANS (1952) outlines the early management of the severely

...ssing is removed after 12–14 days It has given excellent results in 200 cases in the past 2 years, when combined with the intelligent use of

chemotherapy and a suitable diet. Exposure treatment has also been used for 40 patients during the same period. Superficial (and even deep) second-degree burns heal rapidly by either method. Infection of deep burns is less obvious by the exposure treatment, but immobilization and the attainment of a dry wound in encircling burns is difficult. Separation of burn slough is more rapid by the closed method, which should always be used in burns of the hands. Treatment with ACTH has not produced any dramatic or unexpected recoveries

Third-degree burns

Skin-grafts: effect of ACTH.—The effect of administering adrenocorticotropic hormone (ACTH) on the survival of homografts has been studied by BUTTERFIELD, WILLIAMS and EVANS (1952). The investigation was carried out on 3 patients with extensive third-degree burns involving the trunk and thighs. The group comprised an adult male, an adult female and a female child; no patient had previously received treatment with either ACTH or any adrenocortical hormone, and all had adequate adrenocortical reserves. Homografts were implanted, and these were examined and photographed when the burn was dressed. Bacteriological cultures were taken whenever the burns were dressed, or at other convenient intervals. Assessment of adrenocortical function was made, in each case, by laboratory studies and clinical observations The results of the study showed a good adrenocortical response in each instance, and in 2 cases the homografts survived for an unusually long period, all of them, however, deteriorated eventually, and showed no sign of permanent survival There appeared to be a relation between the length of survival and the intensity of adrenocortical response. ACTH therapy did not prevent bacterial invasion or the clinical signs of infection; high granulations grew over the burned areas. There was no increase in the percentage "take" of delayed autografts. Complications of ACTH treatment, including glycosuria and mental disorientation, were observed. It is concluded from the study that ACTH prolongs, but does not perpetuate, the survival of homografts, and that early skin closure is still as urgent as it was before the discovery of this hormone.

Flash burns

Classification of degree [illegible]
flash burns produced by [illegible]
fied 24-inch United Stat [illegible]
violet, 40 per cent visibl [illegible] placed in front of the secondary
[illegible] intensities (1·8–34 calories
[illegible] of the burns was arbitrarily
[illegible] appearance of the burns after 24 hours. A ++++
[illegible]
by 3 calories per square centimetre. Macroscopical examination of the lesions after 24 hou[illegible] was found to be a reliable means of grading the burns

Ocular burns

Corrosion caused by quick-lime, treatment.—WAGENAAR (1952) describes a case of ex- [illegible]
[illegible] from
[illegible] after
[illegible] rs that
[illegible] duced
[illegible]

combined with oil of vitamin A and mydriatics. Severe corneal turbidity is treated by paracentesis, followed, if necessary, by irrigation of the anterior chamber of the eye.

Butterfield, W. J. H., Williams, A. M., and Evans, E. I. (1952). *Lancet*, 1, 737.
Evans, E. I (1952). *Surg. Gynec Obstet.*, 94, 273.
Morton, J. H., Kingsley, H. D, and Pearse, H. E. (1952) *Surg. Gynec Obstet.*, 94, 317.
Wagenaar, J. W. (1952) *Brit. J Ophthal*, 36, 202.

COLITIS

See also B S.P., Vol 3, p 88, S. Key 97

Chronic ulcerative

Diagnosis and treatment

Medical and surgical—Butler (1952) describes the modern treatment of ulcerative

ulcerative colitis. Granular proctitis may be mistaken for mild ulcerative colitis, but the

ance of the bowel are valuable aids to the correct diagnosis Bacteriological examination of the stools should also be carried out to exclude amoebic or bacillary dysentery. In the medical treatment, blood transfusions and the control of secondary infections by the administration of penicillin, combined with one of the insoluble sulphonamides, Chloromycetin, chloram-

ileostomy bag, and may be followed by a two-stage colectomy Indications for surgical treatment are (1) severe or repeated haemorrhage, (2) increasing toxaemia, (3) stricture formation and (4) progressive ulceration of the skin Right-sided colitis, as described by Crohn and his colleagues, might be included in this group. The disease is marked by severe constitutional symptoms, pus in the stools and arthritis Often the ileum is also involved, and it may be impossible to differentiate between regional ileitis and a pure colitis. The treatment of right-sided colitis is usually surgical

Surgical treatment

Indications and results—Gabriel (1952) discusses the surgical treatment of chronic ulcera-

follows 6 per cent for ileostomy, 6 25 per cent for subtotal colectomy; and none for the

rectal segment.

effective measure is removal of the diseased ...

... protein loss and toxic abs ... stage operations. The post-operative ... is lowered A one-stage resection ha ... deaths; none was attributable to the ...

Advances in procedure.—Advances in colonic and rectal sur(... (1952) As a result of various factors, surgery in these regio... radical and more successful (1) Pre-operat... complications, include ... graphy with contrast e... proteins, fluids and elect... tive colitis (d) ... of anaestl... with a sur... and pain ... as diffuse ... good results. (3) the avoidance of complications ... (b) bladder and renal dysfun... care of the colostomy. (a) th...

... ...examination of th... ...should receive greater attention than has been gi...

Butler, E. C. B (1952). *Med. Pr.*, 228, 113.
Gabriel, W. B. (1952) *Brit med J.*, 1, 881.
Ripstein, C. B , Miller, G G., and Gardner, C. McG. (1...
Whipple, A O. (1952) *Canad med. Ass. J.*, 66, 116

COLON—CARCINOMA OF

See also B S.P., Vol 3, p 103, S. Key 98.

Aetiology

Polyposis

Malignancy following treatment.—...

cases, 14 we... be invasive ... longer, 2 pa... of the colon.

Fisher, E. R., and Turnbull, R. B., Jun. (1952). *Surg. Gynec. Obstet.*, 94, 619

CONJUNCTIVA—DISEASES AND INJURIES

See also B S P., Vol 3, p 148, S Key 101.

Cysts

formed when the aqueous humour escapes under the conjunctiva in cases of ulcerative or traumatic perforation, and (2) from cystoid formations, occurring in operation scars, as, for example, after trephination for glaucoma.

Perkins, E W. (1952) *Amer J. Ophthal*, 35, 196

CORNEA—DISEASE AND INJURIES

See also B S P , Vol. 3, p 183, S. Key 104

Experimental and clinical infections

Efficacy of streptomycin

Concentration levels attained—SORSBY, UNGAR and BAILEY (1952) investigate the levels of concentration of streptomycin which can be reached in the eye by systemic and subconjunctival injection, and evaluate the efficacy of streptomycin in experimental infections of the cornea and its use clinically in tuberculous lesions of the eye and in infections by Gram-

in adrenaline, 1 . 1,000, instead of water, for subconjunctival injection Experimental corneal infections with *Pseudomonas pyocyanea* were fully controlled by a single subconjunctival injection of the latter solution For clinical purposes, streptomycin, to be injected subconjunctivally, should be

1 . 1,000, are freshly addec

and acute conjunctival ı

conjunctival injection, a

temically, streptomycin proved helpful in tuberculous keratitis and conjunctivitis and in a case of acute dacrocystitis due to *Proteus vulgaris* The antibiotic gave poor results in cases of presumed tuberculous iridocyclitis, Eales' disease and scleromalacia perforans In phlyctenular ophthalmia, streptomycin treatment tended to cut short severe attacks, and it probably reduced the frequency and severity of relapses

Sorsby, A , Ungar, J , and Bailey, N L. (1952) *Brit med J.*, 1, 119.

DIABETES MELLITUS IN RELATION TO SURGERY

See also B S P , Vol 3, p 250, S Key 108

Management for surgical operations

Pre-operative insulin recommendations

ROLLAND (1952) reports on diabetes mellitus in surgical cases, referring to a series of 300 cases treated over a 2-year period. Most of the patients were over 55 years of age when they required surgical treatment, and a considerable proportion were over 70 years. Few were young subjects The author gives a Table showing the incidence of some of the conditions

effective mea...
degener
primary
The adv
blood ar
stage op
is lowere
deaths, non
deaths m
colectomy
total one-
The indic
ing, (2) st
tinued tox
patients in
demonstra
has usually

Advances in procedure.—Advances in colonic and rectal surgery are discussed by WHIPPLE (1952). As a result of various factors, surgery in these regions has been made safer, more radical and more successful. (1) Pre-operative study and care, to prevent mistakes and complications, include (*a*) adequate examination in all cases of rectal bleeding; (*b*) radiography with contrast enemas; (*c*) correction of anaemia, mal... proteins, fluids and electrolytes—espe... tive colitis, (*d*) proper emptying a... of anaesthetic and of operative pr... with a single hepatic metastasis, b... and pain. Radical resection and ... as diffuse polyposis ... the avoidance of cor... (*b*) bladder and renal ... care of the colosto... necessary, (*b*) pat... in their need for ... the colon until th... a phase which ...

Bu...
Ga... 228, 113.
Ripstein, C. B. (1952). *Brit. med. J.*, 1, 881.
Whipple, A. O. (1952). *Canad. med. Ass. J.*, 66, 116.
... Miller, G. G., and Gardner, C. McG. (1952). *Ann.*

COLON—CARCINOMA OF

See also B.S.P., Vol. 3, p. 103, S. Key 98.

Aetiology

Polyposis

Malignancy following treatment.—FISHER and TURNBULL (195...) ... observations of a series of carcinoma... or papillomatous polyps, whic... of radon seeds) and which w... were 35 cases wh... avera... or se... consi... Swint... descri... cases, ... be inv... longer, ... of the ... the polyp occurred, but ... cases of superficia... to a second lesion ... were treated by abdomino-perineal resectio... but none of the recu... all of which showed invasive carcinoma. Th... carcinoma *in situ* or superficial carcinoma ...

Fisher, E. R, and Turnbull, R. B, Jun (1952). *Surg. Gynec. Obstet.*, 94, 619

CONJUNCTIVA—DISEASES AND INJURIES

also B S P., Vol 3, p. 148, S. Key 101

ts

bus The cyst was removed intact, under local anaesthesia, and had not recurred 1 year r. Examination showed the cyst to be thin-walled and loculated, and to contain clear coid fluid, it was lined by flattened squamous epithelium, supported by thin connective ue. The author points out that these cysts have to be differentiated (1) from pseudo-cysts, med when the aqueous humour escapes under the conjunctiva in cases of ulcerative or umatic perforation, and (2) from cystoid formations, occurring in operation scars, as, example, after trephination for glaucoma.

Perkins, E W. (1952) *Amer J Ophthal*, 35, 196.

CORNEA—DISEASE AND INJURIES

e also B.S P, Vol 3, p. 183, S. Key 104.

perimental and clinical infections

ficacy of streptomycin

Concentration levels attained —SORSBY, UNGAR and BAILEY (1952) investigate the levels of ncentration of streptomycin which can be reached in the eye by systemic and subconjuncal injection, and evaluate the efficacy of streptomycin in experimental infections of the rnea and its use clinically in tuberculous lesions of the eye and in infections by Gram-

tra-ocular concentrations and longer persistence occurred when streptomycin was dissolved adrenaline, 1 · 1,000, instead of water, for subconjunctival injection Experimental corneal fections with *Pseudomonas pyocyanea* were fully controlled by a single subconjunctival jection of the latter solution For clinical purposes, streptomycin, to be injected sub-

case of acute dacrocystitis due to *Proteus vulgaris* The antibiotic gave poor results in cases f presumed tuberculous iridocyclitis, Eales' disease and scleromalacia perforans. In phlycnular ophthalmia, streptomycin treatment tended to cut short severe attacks, and it probably duced the frequency and severity of relapses.

Sorsby, A, Ungar, J, and Bailey, N L. (1952) *Brit med J.*, 1, 119.

DIABETES MELLITUS IN RELATION TO SURGERY

ee also B S P, Vol 3, p. 250, S Key 108

Management for surgical operations

re-operative insulin recommendations

ROLLAND (1952) reports on diabetes mellitus in surgical cases, referring to a series of 300 ases treated over a 2-year period. Most of the patients were over 55 years of age when they equired surgical treatment, and a considerable proportion were over 70 years. Few were oung subjects The author gives a Table showing the incidence of some of the conditions

FACIAL PALSY

See also B.S.P., Vol 4, p. 1, S. Key 147.

Idiopathic paralysis

Symptoms

A follow-up study of 209 cases of so-called idiopathic peripheral paralysis of the facial nerve is presented by MULLER (1952) All the patients were under 40 years of age at the time of first admission to hospital, they had then paralysis of not more than 14 days' duration, without any other pathological changes in the nervous system; 15 had had at least 1 previous attack. Symptoms which may have been manifestations of disseminated sclerosis were ob-

Recurrent cases showed, relatively frequently, oedema of the face, or plicated tongue, or both these symptoms together; various combinations of symptoms may be found in a single family. Conservative treatment by electrical stimulation, in the present series, gave satisfactory results in 97 per cent of the cases, either producing complete return of function, or leaving the patients with slight residual signs which caused little inconvenience; this is taken to indicate that surgical measures are unnecessary in an early stage of the disease The author recommends surgical intervention if no improvement is obtained after 9 months, because no significant spontaneous regression can be expected after that time, recurrences should be given the same treatment as for attacks occurring for the first time

Traumatic palsy

corrective measure, but also to aid in psychological rehabilitation, post-operative photographs of, or personal interviews with, patients who have had similar defects corrected, have been found most helpful in rehabilitation Information as to the time at which the paralysis occurred is regarded as of greater importance than the cause of the injury, in post-operative cases the surgeon's explanation for the injury will help in formulating a plan of treatment Radiography, electrical reactions, and tests for taste or lacrimation, are usually of little value in localizing the injury or in managing the paralysis; they should, however, be performed, with the history and clinical examination in mind Observation and manipulation of the palsied side may indicate the prognosis, cases with slight asymmetry in repose, without atrophy about the eye, and with

cranial nerve

Aetiology and treatment

which called for surgical treatment in this series of cases. They include such conditions as [illegible]

period. In certain cases it [illegible]

[illegible]

Rolland, C. F. (1952). *Brit med. J.*, 1, 737

EAR—EXTERNAL EAR

See also B S.P., Vol. 3, p. 286, S Key 112

Painful helicine nodules

Pathology and treatment

THOMETZ (1952) discusses "painful ear nodule", which is a small keratotic lesion on the edge of the superior and transverse part of the helix The patient usually seeks advice because of pain severe enough to interfere with sleep The lesion is usually mistaken for carcinoma, because recurrence commonly follows removal The disorder was originally named chondrodermatitis nodularis chronica helicis The author illustrates his article with 5 case-reports [illegible] changes [illegible] ficial [illegible] ained [illegible] The [illegible] nges [illegible] f the nodule. The appearance, location and tenderness of the nodule differentiate it adequately from carcinoma. The author found that immediate treatment by electro-coagulation avoided the deformity and painful recurrences commonly associated with excision biopsy.

Thometz, R. W. (1952), *Arch. Otolaryng , Chicago*, 55, 153.

EAR—INTERNAL EAR, ACUTE INFECTION

See also B.S.P , Vol 3, p. 291, S Key 113.

Vascular tumours

Malignant glomus jugulare

[illegible] of the middle ear are prob- [illegible] dimension, with numerous epithelioid cells between them. The glossopharyngeal [illegible] gangliomas or tympanic-body tumours The author describes several cases, [illegible] lasting perhaps for years [illegible] cases vertigo is noted. [illegible] e malignancy was suspected, for growth is slow. Complete excision is desirable, because diagnosis is so difficult. In some cases post-operative *radiotherapy has been useful and may be the only treatment* [illegible] Radical mastoid operations have [illegible] ive. A considerable pro- [illegible] fatal.

Capps, F C W. (1952). *J. Laryng.*, 66, 302.

FACIAL PALSY

See also B.S.P., Vol. 4, p. 1, S. Key 147.

Idiopathic paralysis

Symptoms

A follow-up study of 209 cases of so-called idiopathic peripheral paralysis of the facial nerve is presented by MULLER (1952) All the patients were under 40 years of age at the time of first admission to hospital; they had then paralysis of not more than 14 days' duration, without any other pathological changes in the nervous system; 15 had had at least 1 previous attack Symptoms which may have been manifestations of disseminated sclerosis were observed in 3 cases; Bell's palsy is therefore regarded as very seldom dependent on disseminated sclerosis, although some cases of the disease are initially manifested by facial paralysis All the cases were followed up for 10 years and 40 per cent of them for 16–20 years Cases observ
to f
Rec
both these symptoms together, various combinations of symptoms may be found in a single family. Conservative treatment by electrical stimulation, in the present series, gave satisfactory results in 97 per cent of the cases, either producing complete return of function, or leaving the patients with slight residual signs which caused little inconvenience; this is taken to indicate that surgical measures are unnecessary in an early stage of the disease. The author recommends surgical intervention if no improvement is obtained after 9 months, because no significant spontaneous regression can be expected after that time, recurrences should be given the same treatment as for attacks occurring for the first time.

Traumatic palsy

Management and surgical treatment

LATHROP (1952) discusses the management of patients with traumatic lesions of the facial nerve. Although the incidence of facial palsy following mastoid surgery has decreased, with the advent of the sulphonamides and antibiotics, its occurrence from other causes has increased These newer factors include: (1) surgical extirpation of neoplasms; (2) lacerations or fractures due to automobile accidents, (3) war wounds Every effort should be made, on examination, to assess the injury to the facial nerve, not only to indicate the appropriate corrective measure, but also to aid in psychological rehabilitation; post-operative photographs of, or personal interviews with, patients who have had similar defects corrected, have been found most helpful in rehabilitation Information as to the time at which the paralysis occurred is regarded as of greater importance than the cause of the injury, in post-operative cases the surgeon's explanation for the injury will help in formulating a plan of treatment Radiography, electrical reactions, and tests for taste or lacrimation, are usually of little value in localizing the injury or in managing the paralysis, they should, however, be performed, with the history and clinical examination in mind. Observation and manipulation of the palsied side may indicate the prognosis, cases with slight asymmetry in repose, without

end-to-end suture, (3) nerve grafting, or (4) anastomosis of the facial nerve to an adjacent cranial nerve

Aetiology and treatment

Facial-nerve decompression

BUNNELL (1952) presents a summarized review of papers on the management of facial

... per cent, representing more serious cases, it should be ...

which called for surgical treatment in this series of cases They include such conditions as

time of their admission to the surgical ward The patients were dieted during the post-operative period In certain cases it was necessary to supply carbohydrate by the intravenous infusion of glucose solutions for the first few days after the operation Until a normal diet was taken, soluble insulin was used and long-acting insulin was avoided When the patient was able to take his usual food, protamine-zinc insulin was recommended The author concludes by

Rolland, C. F. (1952). *Brit. med J.*, **1**, 737.

EAR—EXTERNAL EAR

See also B S P , Vol 3, p 286, S. Key 112.

Painful helicine nodules

Pathology and treatment

THOMETZ (1952) discusses "painful ear nodule", which is a small keratotic lesion on the

dermatitis nodularis chronica helicis The author illustrates his article with 5 case-reports

Swedish investigators report a high incidence of frost-bite preceding the occurrence of the nodule The appearance, location and tenderness of the nodule differentiate it adequately from carcinoma. The author found that immediate treatment by electro-coagulation avoided the deformity and painful recurrences commonly associated with excision biopsy.

Thometz, R W (1952), *Arch Otolaryng , Chicago*, 55, 153.

EAR—INTERNAL EAR, ACUTE INFECTION

See also B S P , Vol. 3, p. 291, S Key 113.

Vascular tumours

Malignant glomus jugulare

Pathology —In the opinion of CAPPS (1952), vascular tumours of the middle ear are prob-

the latter even as far distally as where the mastoid canaliculus crosses the

non-chromaffin para-

most

ears

oted.

s sus-

icult.

pected, for growth is slow. Complete excision is desirable, because

may be the only treatment

cal mastoid operations have

tensive. A considerable pro-

ually fatal.

Capps, F. C. W. (1952). *J. Laryng* , 66, 302.

FACIAL PALSY

See also B.S.P., Vol. 4, p. 1, S. Key 147.

Idiopathic paralysis

Symptoms

A follow-up study of 209 cases of so-called idiopathic peripheral paralysis of the facial nerve is presented by MÜLLER (1952) All the patients were under 40 years of age at the time of first admission to hospital; they had then paralysis of not more than 14 days' duration, without any other pathological changes in the nervous system, 15 had had at least 1 previous attack. Symptoms which may have been manifestations of disseminated sclerosis were observed in 3 cases; Bell's palsy is therefore regarded as very seldom dependent on disseminated sclerosis, although some cases of the disease are initially manifested by facial paralysis. All the cases were followed up for 10 years and 40 per cent of them for 16–20 years Cases observed for 15 years showed recurrence in 13 per cent. Recurrent paralysis showed a tendency to familial incidence, but recurrence did not appear to be correlated to the patient's age. Recurrent cases showed, relatively frequently, oedema of the face, or plicated tongue, or both these symptoms together, various combinations of symptoms may be found in a single family. Conservative treatment by electrical stimulation, in the present series, gave satisfactory results in 97 per cent of the cases, either producing complete return of function, or leaving the patients with slight residual signs which caused little inconvenience; this is taken to indicate that surgical measures are unnecessary in an early stage of the disease. The author recommends surgical intervention if no improvement is obtained after 9 months, because no significant spontaneous regression can be expected after that time, recurrences should be given the same treatment as for attacks occurring for the first time.

Traumatic palsy

[illegible]

graphs of, or personal interviews with, patients who have had similar defects corrected, have been found most helpful in rehabilitation Information as to the time at which the paralysis occurred is regarded as of greater importance than the cause of the injury; in post-operative cases the surgeon's explanation for the injury will help in formulating a plan of treatment

[illegible]

[illegible] end-to-end suture, (3) nerve grafting, or (4) anastomosis of the facial nerve to an adjacent cranial nerve

Aetiology and treatment

[illegible]

[illegible] per cent, representing more serious cases. It should be performed at once, not

decompression in late cases vary with the amount of damage to the nerve. Signs of partial nerve damage or of recovery are virtually the same; they comprise (1) muscle tone, (2) symmetry, (3) holding a position after placing, (4) resistance on pulling, (5) warmer feeling,

suture is needed unless nerves can be laid together in a channel. The sural nerve is preferred for grafting.

Bunnell, S (1952) *Arch. Otolaryng., Chicago*, **55**, 417.
Lathrop, F. D (1952). *Arch. Otolaryng., Chicago*, **55**, 410.
Muller, R. (1952) *Acta med. scand*, **142**, 284

FALLOPIAN TUBES

See also B S.P., Vol. 4, p. 37, S. Key 149.

Tumours

Primary carcinoma

Aetiology and treatment—Primary carcinoma of the fallopian tube is discussed by Johnson and Amos (1952), on the basis of the literature and of 1 personal case. The disease is rare, and is seldom diagnosed pre-operatively; it is the most malignant of body cancers It

sterility in patients of child-bearing age

are fairly constant include vaginal dis

and abdominal enlargement. Usually a

cases, is present in one or both adnexal regions. A 40 per cent 5-year survival rate has been

before completing the operation has been suggested, but the authors consider that this procedure would create the possibility of surgical metastases

Johnson, M E K, and Amos, T G. (1952) *Amer J. Surg.*, **83**, 35.

FOOT—SURGERY OF

See also B.S.P, Vol. 4, p 132, S Key 156

Hallux valgus and hallux rigidus

Treatment

The

also

the

interphalangeal joint proximally to about the centre portion of the first metatarsal bone A shorter incision may be made over the joint, with a small separate plantar incision for

Flat foot

Surgical treatment

reviewed; the majority had previously been fitted with corrective shoes, arch supports or Thomas heels The defect was unilateral in 4 cases and 49 were bilateral The series comprised 26 males and 27 females. In 17 feet there was spastic eversion, the remainder being weak, relaxed or pronated feet and the condition being of congenital origin; Kohler's disease was present in 7 cases and 11 children had accessory navicular bones. A total of 111 surgical procedures were carried out. The results of arthrodesis of the talo-navicular and naviculo-

operation was subsequently abandoned. A "double arthrodesis", of the subtalar and talo-clavicular joints was used on 24 feet (6 with section of peroneal tendons and 2 with lengthening of heel-cords) and proved to be a satisfactory operation. A "modified Hoke" operation was performed 27 times, and a standard Hoke triple arthrodesis 26 times. The authors consider the results of various arthrodesing operations to be most successful when the subtalar joint is included

Club-foot

Treatment

Tibialis anterior tendon transference.—CRITCHLEY and TAYLOR (1952) have treated 22 cases of relapsed club-foot by transfer of the tibialis anterior tendon The ages of the patients ranged from 3 to 13 years and the cases were followed up for between 6 months and 4 years. Most of the patients had previously undergone plantar fasciotomy, Steindler's operation, elongation of the tendo calcaneus, or some other operation. The best age for the operation is 3–6 years, secondary changes in soft tissues and bones, after the age of 6 years, prevent adequate correction Because a tendon transplant will not correct a fixed deformity, it may

immobilization

Crego, C H , and Ford, L T. (1952) *J Bone Jt Surg* , 34A, 183.
Critchley, J. E , and Taylor, R. G (1952). *J Bone Jt Surg* , 34B, 49
Mckeever, D C (1952). *J Bone Jt Surg* , 34A, 129.

FROST-BITE

See also B.S P , Vol 4, p 232, S Key 160

Surgical treatment

Sympathectomy

End-results—SHUMACKER (1951) discusses sympathectomy in treatment of frost-bite. Altered vasomotor function not infrequently occurs as a more or less permanent sequel to injury done by
after exposure t
ment An analy
injury was caus
actual freezing

may be useful in early treatment of certain cases, but that additional careful observations are needed for confirmation

Shumacker, H B (1951). *Surg. Gynec. Obstet*, 93, 727.

GALL-BLADDER AND BILE PASSAGES

See also B S P, Vol 4, p. 238, S. Key 161

Biliary-tract disorders

Surgical treatment

radiographically; (6) attacks of subacute pancreatitis; (7) discharge of muco-pus or bile after bili

of pristin

ducts, or

or thicke

(6) sediment or muco-pus

"pseudo–gall-bladder" and

the author's hands, to be

bile-duct is ensured by the

1 when a probe cannot be

passed into the duod

important aspect of

exposure, a well-illu

require intensive pr

maining portions of

Axial union preserv

Surgical decompression

duct system and left

r the catheter, which

atheter is eventually

he method provides

cases with minimal

ed surgical measures

are inapplicable.

Acute inflammatory conditions

Indications for cholecystectomy

HOLDEN, CEBUL and LOUGHRY (1952) discuss the management of acute disorders of the biliary tract. A series of 1,523 cholecystectomies, performed during a period of 10 years, included 20 perforations, of which 17 were local and 3 occurred freely into the peritoneal cavity; this is an incidence of 1·3 per cent. The 3 free perforations occurred in acute cases, in 2 instances apparently before the patient was admitted to hospital. 1 of the 3 patients died Of the 17 localized perforations, 6 were in acute cases and 11 in chronic cases. The 9 perforations in 315 acutely inflamed gall-bladders represent an incidence of 2 8 per cent. The authors' conservatism in operating in acute cases is doubtless due largely to the low incidence of perforation in their series, and also to the fact that only 1 patient in 1,523 died as a result of perforation. The series showed an over-all mortality rate of 1·1 per cent. Since 1945 (the middle of the period of the study), 4 of the 17 deaths have occurred, a mortality rate of 0 5 per cent; 3 deaths followed removal of acutely inflamed gall-bladders; 1 death resulted from a residual stone in the common duct, and 2 from severe gastric dilatation and ileus; the fourth patient died from a massive pulmonary embolus after an elective cholecystectomy for cholelithiasis and chronic cholecystitis. In the acute cases in the series the operations took place at times varying from a few hours to several days after admission; 5 of the 8 patients who died after operation for acute cholecystitis were operated on within 72 hours of the onset of the illness. The conclusion drawn by the authors from the data and mortality figures in this study is that, if the proper indications exist for either cholecystectomy or cholecystostomy, the interval between the onset of the attack and the operation is of little consequence, and that any delineation of a critical period in which surgery may or may not be performed is not in the patient's best interest. The authors consider that a larger number of patients with demonstrable biliary calculi should be advised to have an elective cholecystectomy.

Cholelithiasis

Predisposing factors

Clinical survey.—LITTLER and ELLIS (1952) present a clinical survey of gall-stones Con-

[illegible]

this connexion led the authors to make the present investigation An analysis was made of [illegible] period, [illegible] tions on [illegible] obesity and familial predisposition made by other observers The sex and age incidence in this disease closel[illegible] is known to [illegible] lithogenous [illegible] indicated tha[illegible] gall-bladder dyspepsia. A more careful assessment should be made of the pain described by the patient, the authors emphasize this by using the term, minor colic, by which they mean a right subclavian pain of considerable severity, occurring with significant frequency It is admitted, however, that cases will still remain in which gall-stones will be discovered by accident, and in which the question of whether or not the stones are causing the symptoms must be carefully considered

Ascending cholangitis and biliary cirrhosis

[illegible]

was anastomosed to the duodenum, in another group to an upper loop of the jejunum, and in a third group to a Roux-Y loop of jejunum One dog from each group was sacrificed 6 months after and the

rest between 7 and 30 months after the anastomosis was made. Anastomotic stricture

when the common duct was anastomosed to the duodenum rather than to a jejunal loop

Hayes, M. A , and Coller, F. A (1952). *Ann Surg* , 135, 98.
Holden, W. D , Cebul, F A , and Loughry, C W. (1952). *J. Amer. med Ass.*, 148, 879
Littler, T. R., and Ellis, G. R (1952). *Brit med. J* , 1, 842
Maingot, R. (1952) *Ann. R. Coll Surg., Engl* , 10, 97.
Musgrove, J E., Grindlay, J H , and Karlson, A G (1952). *Arch. Surg., Chicago*, 64, 579.

HAEMORRHAGE

See also B.S P , Vol 4, p 378, S. Key 177.

Idiopathic thrombopenic purpura

Effects of ACTH and cortisone on the platelet count

resistance test Poor contractility of capillaries is a feature of thrombocytopenic purpura

capillaries. Treatment when the blood vessels are at fault is limited to splenectomy, if this is *appropriate, and transfusions of fresh blood* *Defects of the coagulation mechanism* are responsible for haemophilia, which is now believed to be due to a congenital deficiency of a

missing factor, such as vitamin K, and applying thrombin, plasma or fibrin foam locally. Whitby emphasizes the effectiveness of fresh as compared with stored blood for transfusions.

Whitby, L (1952) *Practitioner*, 168, 216

HAND

See also B.S.P., Vol. 4, p 386, S Key 178.

Reconstruction of the thumb

Choice of method

Absence or presence of functional stump.—Reconstruction of the thumb is discussed by Sanders (1952) A satisfactory thumb substitute must be capable of a fair degree of skill and power in pinching, grasping and opposition, which are the fundamentals of thumb

rophic
ntable.
tional
ce of a

A useful stump should be so elongated
the adjacent digit; excessive length gives
scular impairment and sensory inadequacy
which reconstruction was achieved satis-
pedicle-flap transfer.

Sanders, G B (1952) *Amer. J. Surg* , 83, 347

HERNIA

See also B S.P., Vol. 4, p. 428, S. Key 180.

Oesophageal hiatus hernia

Operative procedure

The transthoracic approach —A series of 111 consecutive cases of oesophageal hiatus hernia of the diaphragm, operated upon by the transthoracic approach, are reviewed by SWEET

4 were

g types:

ormerly

lly short

were of

stomach,

ach

ples

unrelieved, there were 2 cases of proved recurrence, and 1 patient was not traced

Sweet, R H (1952) *Ann Surg*, 135, 1.

KIDNEY AND URETER—GROWTHS

See also B S P, Vol 5, p. 268, S Key 210

Malignant tumours

operation Anaesthesia for arteriography is provided in most instances by 0 5 gramme of thiopental sodium, spinal anaesthesia is recommended for removal of tumours Renal neoplasia should be treated by nephrectomy Irradiation will shrink a Wilms' tumour, but does not, by itself, destroy all the neoplastic cells Irradiation, in a boy aged 8 years, was followed by scoliosis, owing to the failure of the irradiated tissue to grow with the remainder of the body.

Late metastasis from renal carcinoma

STARR and MILLER (1952) report on a case of renal carcinoma, in which metastasis was disclosed 20 years after the removal of the primary tumour. The solitary polypoid jejunal metastasis gave rise to anaemia and occult bleeding in the stools An additional aspect of

d

s

t

Nelson, O. A., and Mousel, L. H. (1952). *J. Amer. med. Ass.*, 148, 171.
Starr, A., and Miller, G. M. (1952). *New Engl. J. Med.*, 246, 250.

LARYNX—SURGICAL DISEASE OF

See also B S.P., Vol 5, p. 338, S. Key 216.

Malignant disease

Treatment

Treatment was completed in 62 of these 69 cases, which were almost equally divided between intrinsic and extrinsic lesions The disease in 31 cases was clinically arrested, but 16 of these patients died of intercurrent diseases prior to the lapse of 5 years, and 2 were lost to the follow-up. Thus of the 62 cases 44 remained, in which there was a relative cure rate of 30 ... xtrinsic, ... d well 5 ... was 80 ...

Garland, L. H , and Sisson, M A (1952). *Surg. Gynec. Obstet.*, 94, 598.

LIVER—CIRRHOSIS

See also B S P., Vol 5, p 437, S. Key 223.

Portal hypertension

Treatment

Porta-caval anastomosis—The value of side-to-side porta-caval anastomosis has been ... performed on 12 ... side-to-side ... was ... nous ... tion, ... with ... both haemorrhage and ascites. ... follow an adequate medical regimen The shunt operation, in addition, is stated to be likely to eliminate the ever-present possibility of death from haemorrhage.

Large, A , Johnston, C G , and Preshaw, D. E. (1952). *Ann. Surg.*, 135, 22.

LUNG—TUMOURS

See also B.S.P., Vol. 5, p. 450, S. Key 225.

Cancer of the lung

Carcinoma

Morbid anatomy—Borrie (1952) reports on a series of 1,800 patients with primary carcinoma of the lung, seen from 1933 to 1951, of whom 45 per cent were treated surgically, 19 per cent of the total being subjected to lung resection. The author analyses the factors affecting the prognosis in the latter group, 94 per cent of whom were males Of the resected lungs 200 were dissected and approximately 5 lymphatic glands from each were sectioned. The neoplasms were divided into (1) epidermoid carcinomas (68 per cent), (2) adenocarcinomas

(27·5 per cent) and (3) undifferentiated types (4 5 per cent). The position of the main lymphatic glands draining the two lungs is detailed and the incidence of secondary involvement

in only 42·5 per cent and only 1 adenocarcinoma had produced metastases. Most of the deaths from secondary deposits occurred within a year of operation; it is therefore concluded that "cure" cannot be claimed before 3 years have elapsed. The outlook is worst for undifferentiated growths, 6 out of the 9 patients dying from metastases in the first post-operative

pain in inoperable cases Eight growths were detected during mass radiography, these were peripheral in situation, and therefore silent until far advanced Post-operative deaths are analysed: pyothorax without bronchial fistula and massive pulmonary embolism were the commonest fatal complications, bronchial fistulae occurring whether or not the growth had invaded the site of bronchial section. Borrie concludes that the chances of survival in lung cancer are unpredictable, for blood-borne metastases, rarely detectable pre-operatively, may always have occurred even in apparently early cases

Borrie, J. (1952) *Ann R. Coll Surg., Engl*, 10, 165.

LUPUS VULGARIS

See also B S P., Vol 5, p 476, S Key 226

Lupus erythematosus

stage of phlebitis was observed in 2 cases of lupus erythematosus and in 1 case of the control group, the latter being a case of operative shock (2) The cellular reactive phase, consisting

Lowman, E W , and Slocumb, C H (1952) *Ann intern Med*, 36, 1206.

MEDIASTINUM

See also B.S P., Vol. 6, p 29, S Key 230

Mediastinal fascia

inaccurate and

of the fascia li

solely pretracheal. It forms a complete investing layer to both trachea and oesophagus It is best described as perivisceral. In the neck the anterior part of this perivisceral fascia is thin and fibrous but becomes thicker and fibro-fatty in nature as it passes into the thorax. Laterally and dorsally the fascia is thinner, is of delicate texture and is continuous above with the

this plane that the cervical and mediastinal structures are generally removed at necropsy In all, 12 heart and lung specimens were treated by subfascial, peritracheal and hilar infiltration in order to demonstrate the extensions of the mediastinal fascia.

Marchand, P (1951) *Thorax, Lond.*, 6, 359.

MELANOMA

See also B S.P., Vol 6, p. 62, S Key 232

Malignant melanoma

Treatment

of malig-
na e series
co ises the
tumour was situated in a local extremity; 29 patients gave a history of a pre-existing benign naevus, and 21 patients described various forms of trauma, which may have constituted the deciding factor in initiating a malignant change. In the management of 26 cases, radium therapy was employed, either alone or combined with surgery. The lesions in the remaining

observed that, in the patients who survived, 12 cases were classified as belonging to stage 1 and only 2 cases belonged to stage 4 A relatively poor prognosis was associated with the advanced stages of the disease, especially in elderly patients with a history of trauma

avoids the mutilation which is produced by excision

Reitman, P. H. (1952) *Amer J Roentgenol*, 67, 286

MOUTH AND PHARYNX, MALIGNANT DISEASE OF

See also B S P, Vol 6, p 82, S Key 234

Hypopharynx

Carcinoma

amous-cell carcinoma of the hypo-
s 18 cases in which radical surgery
the disease
had reached an advanced stage,
hoarseness Several patients suff

al surgery. It was established that
and (2) laryngo-oesophago-pharyng-

Mouth

Upper jaw and nasal sinuses

Malignant tumours and their treatment.—MOFFETT (1952) classifies malignant neoplasms

complete excision of the growth, followed by irradiation. Metastases must first be excluded, although these arise usually only in advanced cases. Pre-operative rest and dental treatment are stressed. Diagrams are included to show the incision and the extent of removal in each type of growth A week after operation maximal irradiation is given; later a permanent denture is fitted. Considering the radical nature of these operations, post-operative disfigurement is stated to be remarkably slight In a series of 20 cases, 16 patients are surviving without recurrence, 12 of these a year or more after operation It is emphasized that such results can be obtained only by a combination of surgery and radiotherapy

Cancer of the gums

sites of involvement, outside the gingivae, were the cheek and the floor of the mouth. Biopsy studies were performed in all cases, with the exception of 2 advanced cases which terminated fatally. All the lesions were relatively low-grade squamous-cell carcinomas, except 1 basal-cell tumour, which had extended through the lower lip to invade the lower jaw and overlying gums The ages of the patients averaged 64 years, over one-third of the number were aged 70 or more years Malignant invasion of underlying bone was noted on admission

irradiation necrosis in which surgical measures are needed The authors point out that radiotherapy can control some cases of malignant invasion of bone, and so avoid the need for resection of the jaw.

Martin, C L., and Craffey, E. J (1952) *Amer J. Roentgenol*, 67, 420.
Moffett, A J (1952) *J Laryng*, 66, 132
Raven, R W (1952) *Brit med J*, 1, 951

NOSE, NASOPHARYNX AND ACCESSORY SINUSES

See also B S P , Vol 6, p 271, S Key 244

Nose

Ulcerative destruction

resistant *Staphylococcus pyogenes*, *Streptococcus haemolyticus* and a non-pathogenic *Cory-bacterium* was isolated. Aureomycin, in doses of 250 milligrams 3-hourly, controlled the spread of the ulcer, but no sign of healing appeared. Repeated cultures revealed a pure growth of *Staph. pyogenes.* Superficial x-ray treatment was twice given and Sulphadimidine tried instead of aureomycin, but the ulcer immediately spread, so that treatment with aureomycin (500 and 750 milligrams 3-hourly) was again instituted. The condition of the ulcerated area improved, but then beca... gramme, followed by 0 5 ... of the ulcer within 1 mo... stitutional disturbances a... leucocytosis A mild recurrence, due to a different strain of *Staph pyogenes*, 2 weeks later, responded at once to chloramphenicol The authors suggest that the condition is a non-specific but unusual response to staphylococcal infection.

Chondrosarcoma

Clinical picture and prognosis.—LAWSON (1952) points out that chondrosarcoma is rare in ...

with large nuclei, or with 2 nuclei, or of any giant cell with large single or multiple nuclei or clumps of chromatin. A woman aged 76 years, suffering from diabetes mellitus and ...

arising from the septum, but for cosmetic and other reasons complete removal was impossible The tissue was identified as a chondrosarcoma Post-operative x-ray therapy was again ...

Intranasal encephaloceles

Diagnosis and treatment—WALKER, MOORE and SIMPSON (1952) survey the problem of intranasal encephaloceles, and make recommendations for reducing mortality. Any nasal ...

mass may ...

... ich affords ... simple and ... whenever ...

Lawson, L. J. (1952) *Arch Otolaryng*, *Chicago*, 55, 559.
Sneddon, I B., and Colquhoun, J. (1952) *Brit. med J.*, 1, 298.
Walker, E., Moore, W. W, and Simpson, J. R. (1952). *Arch. Otolaryng.*, *Chicago*, 55, 182.

OESOPHAGUS

See also B S.P, Vol. 6, p. 314, S. Key 247.

Perforation, accidental

Treatment

Immediate closure.—Although they admit that in treating oesophageal perforations, drainage of the site of the perforation is usually first recommended, WEISEL and RAINE (1952)

describe 7 cases of traumatic oesophageal perforation treated by immediate closure of the perforation by (1) suture as soon as the diagnosis had been made (within 3–38 hours), (2) drainage of the fascial or pleural space, and (3) administration of antibiotic drugs and supportive therapy. The perforations in various sites had resulted from oesophageal instrumentation in 5 of the 7 cases (1 of oesophageal carcinoma) and in the remaining 2 cases from the ingestion of a foreign body by children. The outstanding feature in all the patients was extreme pain, localized to the back or to the back and epigastrium, although respiratory embarrassment predominated in the 2 children and the shock-like state did not fully disappear until the mediastinum was opened. X-rays showed a pneumothorax, with mediastinal widening or emphysema, and the existence of a perforation was proved in 2 cases by oral ingestion of Lipiodol. In addition to closing the perforation with interrupted silk or cotton sutures, a thorough cleansing of the mediastinum and mechanical removal of foreign material and necrotic tissue was performed, and thus appeared to be of value in securing a favourable response. The mediastinal pleura was usually left open to allow drainage into the pleural space. All the patients recovered with apparent healing of the perforation.

Foreign-body invasion

Complications

Mediastinitis.—Mediastinitis, occurring after perforation of the cervical oesophagus by a foreign body, is discussed by Korkis (1952).

open, and the resultant scars in 2 cases have been satisfactory The lower end of the scar in the third case shows some puckering and contraction, but it does not restrict head movements, and a plastic operation is not considered to be necessary

Korkis, F. B. (1952). *Lancet*, **1**, 4
Weisel, W., and Raine, F. (1952). *Surg. Gynec. Obstet.*, **94**, 337

OVARY

See also B.S P., Vol. 6, p. 407, S. Key 254.

Tumours

Carcinoma

Evans, G. M. (1952). *J. Obstet. Gynaec., Brit. Emp.*, 59, 82.

resistant *Staphylococcus pyogenes*, *Streptococcus haemolyticus* and a non-pathogenic *Corynebacterium* was isolated. Aureomycin, in doses of 250 milligrams 3-hourly, controlled the spread of the ulcer, [illegible] of *Staph pyogenes* [illegible] instead of aureomycin [illegible] (500 and 750 milligrams 3-hourly) was again instituted. The condition of the ulcerated area improved, but then became stationary. The treatment was changed to chloramphenicol (1 gramme, followed by 0 5 gramme 3-hourly), which resulted in sterile cultures and the healing of the ulcer within 1 month Throughout the 3 months' illness, the patient was free of con- [illegible] is nor [illegible] later, [illegible] non-specific but unusual response to staphylococcal infection.

Chondrosarcoma

[illegible] or clumps of chromatin A woman aged 76 years, suffering from diabetes mellitus and [illegible] Radio- [illegible]

Intranasal encephaloceles

[illegible] and other neo [illegible] of the nasal s [illegible] visible in [illegible] the pharynx [illegible] hough the [illegible] norrhoea [illegible]

Lawson, L J. (1952) *Arch. Otolaryng., Chicago*, 55, 559
Sneddon, I. B., and Colquhoun, J. (1952) *Brit med J*, 1, 298
Walker, E., Moore, W. W., and Simpson, J. R. (1952) *Arch. Otolaryng, Chicago*, 55, 182.

OESOPHAGUS

See also B S.P, Vol. 6, p. 314, S. Key 247.

Perforation, accidental

Treatment

Immediate closure.—Although they admit that in treating oesophageal perforations, drainage of the site of the perforation is usually first recommended, WEISEL and RAINE (1952)

Constriction

Annular constriction

Treatment.—Annular pancreas.—WAKELEY (1951) reports a case of annular pancreas,

Tumours

Islet-cell tumours

Blood-vessel invasion.—WEBSTER and BLADES (1952) describe a case of an islet-cell tumour of the pancreas, in which hypoglycaemic attacks coincided with the menstrual

the blood vessels

Carcinoma of the ampulla of Vater

Symptoms and signs and treatment.—BEALE and TRULOCK (1952) describe 2 cases of

entiation from a stone impacted in the ampulla and from a benign ampullary tumour; in the second case, duodenotomy differentiated the lesion from carcinoma of the head of the pancreas and from pancreatic fibrosis secondary to recurrent pancreatitis The differentiation

Carcinoma of the pancreas

Diagnosis radiography.—Radiological findings in carcinoma of the pancreas are discussed by BEELER and KIRKLIN (1952) A review has been made of the records of cases in which carcinoma of the pancreas was diagnosed at operation during a period of 4 years; 167 cases,

PANCREAS

See also B.S.P., Vol. 6, p. 433, S. Key 257.

Fibrocystic disease

Neonatal case of perforation with peritonitis

Signs and symptoms.—NASH and SMITH (1952) describe a case of fibrocystic disease of the pancreas, with meconium peritonitis at birth. The infant was a male, and there was normal delivery at term. Abdominal distension was remarkable at birth and rendered palpation impossible. Bowel sounds were absent. The infant passed one mud-coloured meconium stool and vomited once only. Intestinal obstruction was diagnosed, and at operation a large quantity of turbid brown fluid, but no perforation, was found. Death ensued and matting

tracheal glands. The appearance of the exudate in the peritoneal cavity places the perforation at, or shortly before, delivery. As no mechanical cause for the obstruction was found, it is ... artery ... nd in ... It is suggested that the pulmonary findings in this case can be accounted for (1) by an episode of asphyxia shortly after birth, possibly due to aspirated liquor, and (2) by the fact that endotracheal anaesthesia was used at operation.

Aberrant pancreas

... is discussed by ... eater frequency ... rying from 0 04 ... 410 consecutive ... ium in 33 cases, ... e found among ... ie pancreas was found to be normal and of average size and shape. Over 80 per cent of the aberrant nodules were found in the duodenum, within a few centimetres of the site of embryological development of the two *anlagen* of the pancreas. They grow slowly, but tend to become larger with ... Complications ... rant pancreas ... are clinically ... enlargement

(4) ...
Ra ...
aut ...
of ...
considered only as a last resort, the case being re-studied at frequent ...

Traumatic pancreatitis

Causation

... th and without associated injuries, is discussed by MATHEWSON ... it is ... ter-

Constriction

Annular constriction

Treatment.—Annular pancreas.—WAKELEY (1951) reports a case of annular pancreas, in which the patient first came under observation complaining of indigestion Alkaline therapy

The peritoneum on the outer side of the duodenum was sutured and the abdominal wound was closed in layers Recovery was uneventful

Tumours

Islet-cell tumours

Blood-vessel invasion—WEBSTER and BLADES (1952) describe a case of an islet-cell tumour of the pancreas, in which hypoglycaemic attacks coincided with the menstrual periods A girl aged 20 years had had trance-like automatic episodes on the first day of 4 successive menstrual periods. At the time at which her next period was due, she was found in the morning in a semi-comatose state This lasted several hours, but by the afternoon her confusion had cleared She was very restless that night, and the following day was again semi-stuporous but ate normal meals Next day she was quite well, but that night she lapsed into a deep coma, in which she died after admission to hospital, in spite of the administration of glucose *per rectum* and intravenously At necropsy, the pituitary gland was found to be 1½ times the normal size, and it contained a high proportion of eosinophil cells. The pancreas contained a round, dark-red soft, solid tumour, 1·25 centimetres across, which was invading the blood vessels

Carcinoma of the ampulla of Vater

Symptoms and signs and treatment—BEALE and TRULOCK (1952) describe 2 cases of

the true nature of the lesion was ascertained. In the first case, the procedure allowed differentiation from a stone impacted in the ampulla and from a benign ampullary tumour; in the second case, duodenotomy differentiated the lesion from carcinoma of the head of the

the pancreas have a less favourable prognosis, and surgical measures, in some instances, may be merely palliative

Carcinoma of the pancreas

Diagnosis radiography—Radiological findings in carcinoma of the pancreas are discussed by BEELER and KIRKLIN (1952) A review has been made of the records of cases in which carcinoma of the pancreas was diagnosed at operation during a period of 4 years; 167 cases,

in wh ch the

ical findings were positive
, ranged between 2–4 and

(4)
or
(5)
the
ca
of

ie large, and often inoperable,
sion of the duodenum. With
regard to treatment, 9 patients underwent radical pancreato-duodenectomy, and radiological findings were positive in 8 of these cases

Carcinoma of the head

Pancreatico-gastrostomy.—A description of 2 cases, in which pancreatico-gastrostomy was performed successfully for the treatment of carcinoma of the head of the pancreas, is given by DILL-RUSSELL (1952) In the technique used, the pancreatic neck, with its dilated duct,

cision, slightly less than the width
The clamp is temporarily removed
is drawn through the incision by
the stay sutures Interrupted sutures, inserted from inside the stomach, join the pancreatic tissue to the gastric wall The duct, which projects into the stomach, is not sutured, but the stay sutures are used to anchor the pancreatic stump to the posterior gastric wall distally
Silk is regarded as the
the proteolytic enzyme of the pan-
c
o-gastrostomy seems to be the best
n
cases, it cannot affect the ultimate
prognosis

Total extirpation of pancreas

End-results.—WHITFIELD, GOUREVITCH and THOMAS (1952) describe a case in which

ment was 40–60 units. The patient had occasional mild hypoglycaemic reactions, but no more than would have been usual in ordinary diabetes mellitus. There was slight macrocytic anaemia.

Islet-cell adenoma

and syncope. Symptoms related to disturbance of the central nervous system occur, for the
onic or
diagnos-
during
fasting or following severe mental or physical exercise, (2) blood-sugar values below 50

regarded as the procedure of choice when a tumour can be found, either in the pancreas or

in an heteroptopic extra-pancreatic location. If careful search fails to reveal any evidence of an adenoma of the pancreas, adequate subtotal resection of the pancreas is recommended.

Beale, G. L., and Trulock, A. S, Jun (1952). *Amer. J Surg*, 83, 20.

PEPTIC ULCER AND ITS COMPLICATIONS

See also B S P., Vol 6, p. 496, S. Key 262.

Gastro-jejunal

Aetiology and treatment

Treatment of ulceration and fistulation.—AIRD (1952) discusses gastro-jejunal ulceration, which usually follows an operation for a severe degree of duodenal ulceration Its incidence after gastrectomy is probably less than 5 per cent Few of the jejunal ulcers seen today are the result of gastro-jejunostomy, for the operation is seldom performed now for the relief

this condition The complication of

Treatment

Vagotomy—WALTERS, PRIESTLEY and BELDING (1952) give an account of vagotomy in the treatment of gastro-jejunal ulceration. The report is based on 118 cases of gastro-jejunal ulcer, and 4 cases of gastro-duodenal ulcer, in which vagotomy was performed with or without other procedures The transthoracic route was used in 54 cases and the transabdominal in 68 cases. Follow-up data were available in 97 cases, which showed that gastro-jejunal ulceration occurred after gastro-enterostomy in 41 cases, and after gastric resection in 53 cases

patients with gastro-jejunal colic fistula were treated by vagotomy with or without other procedures. The results in these cases were largely good.

Gastric ulcer

Treatment

Gastrectomy and colonic replacement: technique.—Some early results of the radiological investigation of colonic replacement of the stomach are recorded by HARRISON (1952) The operation, in which a length of the transverse colon is substituted for the resected portion of the stomach, aims at alleviating the distressing symptoms which have so often followed, early or late, the Polya type of gastrectomy. A series of 30 cases have been followed up radiologically for 6 months or more. The results demonstrate the value of the technique in the treatment of peptic ulceration and of post-gastrectomy syndromes. The "stomach mechanism" produced has considerable capacity and shows movement; frequent regurgitation of the meal into the stomach, by the colon, ensures some degree of mixing and maceration The intermittent entrance of chyme by the normal route maintains the essential intimate contact of the intestinal contents with the intestinal mucosa. The meal, after operation, normally reaches the ascending colon 6 hours after ingestion. Radiography has not identified the site of the end-to-end anastomosis in the transverse colon, and has shown no alteration of the normal haustral pattern. The only demonstrable effect of removing as much as 7 inches of the colon for interposition between the gastric remnant and the duodenum is a slight lowering of the hepatic flexure This has been observed in every case

Gastrectomy post-operative "dumping" syndrome.—GOLIGHER and RILEY (1952) discuss the incidence and mechanism of the early dumping syndrome after gastrectomy. Although the transient hypoglycaemia which, in many patients, follows the ingestion of food, may be the cause of late postprandial symptoms in some cases, it cannot explain the early dumping syndrome, which is regularly experienced within a few minutes to half an hour after taking food The dumping symptoms have also been ascribed to reflux distension of the proximal [illegible]

[illegible]

gastrectomy. Colon replacement does not eliminate dumping, nor, in the [illegible] reduce it sufficiently to justify use of this method.

Gastric ulcer: perforated

Treatment

[illegible] records 13 cases of acute [illegible] tal gastrectomy (75 [illegible] e mortality was nil. [illegible] vious ulcer histories [illegible] inged from 3½ to 24 [illegible] 1 death The author [illegible] he following criteria [illegible] in gastric surgery. [illegible] blood bank should be available [illegible]

at least up to 10–12 hours; cultures, made in 12 of the present series, all were negative.

would cause narrowing to the point of obstruction.

Gastric and duodenal

Treatment

Gastrectomy and vagotomy.—TANNER (1951) discusses the use of surgery in the treatment of peptic ulcer. Wedge excision is no longer performed, because the operation is inadequate Gastro-jejunostomy is an excellent cure for duodenal ulcer Unfortunately, however, anastomotic ulceration may ensue. Either gastrectomy or section of the vagus nerve is the operation of choice. After partial gastrectomy gastric ulceration is not likely to recur, for the acid level is neutralized by the duodenal juices which are constantly propelled into the stomach Furthermore, the lesser curvature is not exposed to the constant stimulus of a high concentration of acid If an ulcer on the lesser curvature is situated near the cardia the Pauchet method should be employed. The ulcer is included in the resection by removing a tongue-shaped portion of the lesser curvature The Billroth I form of gastrectomy yields good results, and the post-operative symptoms are comparatively mild The mortality rate after gastrectomy

gastrectomy. The duration of this disability is prolonged when the patient continues to take small meals, but the symptoms are relatively mild in the patient who is determined to make a good recovery Biliary regurgitation may also cause discomfort. In 1941–43 Tanner performed partial gastrectomy in 91 cases of duodenal ulcer. Fifty-seven of these patients were completely symptomless five years later. During the period 1941–50, 14 out of 904 patients died after gastrectomy for benign ulcer. Vagotomy was performed in 56 instances, but retention symptoms necessitated further surgical treatment in nearly one-third of the number of cases In patients who had suffered from prolonged obstructions the stomach was found to be adherent to the liver, diaphragm and anterior parietes When vagotomy was combined with either pyloroplasty or gastro-jejunostomy satisfactory results were obtained in 102 out of 116 cases.

Aird, I. (1952). *Med. Pr.*, 227, 199

PHARYNGEAL DIVERTICULA

See also B S P, Vol 7, p 1, S Key 265.

Pharyngo-oesophageal diverticulosis

Surgical treatment

Pre-operative preparation and technique—Cases of pharyngo-oesophageal diverticulosis

muscle is exposed and retracted downwards, the sternomastoid muscle is retracted laterally, and the sternohyoid muscle and thyroid gland are retracted medially. The inferior thyroid vessels are retracted downwards or divided. The carotid sheath is retracted laterally. The

in a series of 7 cases, and complications did not arise.

Janes, E C (1952) *Canad. med Ass J*, 66, 255

PREGNANCY—SURGICAL INTERVENTION DURING

See also B.S.P., Vol. 7, p. 116, S. Key 277.

Ectopic pregnancy

Management

Pre-operative diagnosis and surgical treatment.—CAMPBELL (1952) analyses the management of ectopic pregnancy with special stress on the pre-operative diagnosis in 4 Seattle hospitals in the years 1940–50. The incidence was 1 in 165 live births and the total number of cases 395 A certain number of additional cases are not considered, because either surgical or pathological confirmation of the diagnosis was not forthcoming. Unfortunately the pre-operative diagnosis and the preliminary investigations were not recorded in all cases. Ectopic gestation

pregnancy had an average of 1 6 units of blood each; subsequently 62·5 per cent received an average of 2 1 units each Of the 330 patients operated upon, 60 had additional operations

there had been rupture by the time of operation, 211 were on the right side, and 156 on the left, in 26 cases the location was not recorded. Two patients had bilateral ectopic pregnancies at the time of operation; 16 patients had had an ectopic pregnancy before, which is a recurrence rate of 4 4 per cent Whether or not the free blood in the peritoneal cavity was removed did not appear to make any difference in the post-operative course. There was 1 post-

diagnosis should be sought for Blood transfusion is essential, but the fate of the free blood in the peritoneal cavity may not matter very much

Campbell, R M. (1952) *Amer. J. Obstet. Gynec.*, 63, 54.

PROSTATE

See also B.S P , Vol 7, p. 133, S Key 278.

Prostatectomy

Technique

of choice in
same time.
by Millin,
eration by
ate was as
od surgical
infection

The volume of residual urine cannot be employed as an indicator for operation, since it may vary from day to day. The operative technique used was retropubic prostatectomy; it is pointed out that wedge-shaped excision of the vesical neck was performed only in the presence of fibrous thickening, revealed by digital palpation Among post-operative com-
although.
using the
operation.
ne method
is advocated as a standard one in treating all benign prostatic lesions, though the author does not deny that other methods can be equally effective.

Post-operative complications

Avoidance of urinary obstruction.—In a historical review of urinary obstruction after prostatectomy, WARD and GREEN (1952) first cite the important paper by Thomson-Walker in 1921. With the Freyer operation, stricture was apt to occur if the prostatic bed communi-

cated either with the membranous urethra or, more commonly, with the bladder. Thomson-Walker described the open operation of suprapubic prostatectomy, designed for the preven-

attempted to aid epithelization of the prostatic cavity by drawing down the trigonal end of the bladder. The authors point out that post-prostatectomy obstruction is still not un-

Treatment of strictures below the prostatic level is by regular dilatation; contractures of the

exclude calculi and a catheter tied in.

Ostenfeld, J (1952) *Acta chir. scand*, 102, 447
Ward, R. O., and Green, J. A. S (1952) *Practitioner*, 168, 262.

PULMONARY TUBERCULOSIS

See also B S P., Vol. 7, p. 197, S. Key 281

Surgical treatment

Pneumonectomy and immediate thoracoplasty

Technique.—CRUICKSHANK and PAPAMICHAEL (1951) report on 15 cases of pulmonary tuberculosis treated by pneumonectomy and immediate thoracoplasty The technique begins by placing the patient in the face-down position A thoracoplasty incision is then made and the sixth rib resected subperiosteally The removal of 2 ribs is preferable, especially when it

longer portion of the seventh is resected When the thoracoplasty has been completed, a drainage tube is placed through the ninth intercostal space posteriorly and is connected with a suction pump. A tightly strapped pad is placed in the axilla to control the paradoxical movement and help in obliteration of the space. The drainage tube is removed within 48 hours.

Artificial pneumothorax

Development of haemothorax during refill—MASHITER (1952) has given an account of 3

oscopy cannula can be used Thoracotomy is needed only in cases of serious continued haemorrhage; after it the chances of preserving a pneumothorax are poor. When evacuation

is prevented by clots, the intrapleural injection of streptokinase, followed by aspiration, has given promising results

Cruickshank, G., and Papamichael, E (1951). *Thorax, Lond*, 6, 369.
Mashiter, W. E (1952). *Lancet*, 1, 188.

RECTUM—PROLAPSE

See also B S.P., Vol. 7, p 373, S. Key 293.

Massive prolapse

Treatment

Formation of new pelvic floor.—Ripstein (1952) discusses the treatment of massive rectal prolapse. The condition is a sliding hernia of the anterior wall through a defect in the endopelvic fascia. An adequate procedure must meet the basic requirements of any repair for hernia; in addition, the posterior curve of the sacrum must be restored in order to minimize the effect of increased intra-abdominal pressure. The majority of cases occur in elderly multiparous females; in most instances, the pelvic fascia and the levator muscles are thin and atrophic. The author has treated 4 female patients, whose ages averaged 65 years, by a technique which involves the formation of a new pelvic floor from a graft of fascia lata. A follow-up examination of these cases for 18, 16, 12 and 8 months, respectively, has shown no recurrence, and the patients' symptoms were completely relieved in each instance The sphincter ani begins to regain its tone about 1 month post-operatively, and full continence is restored within 2–3 months.

Surgical treatment

Oil-soluble anaesthetics and lasting analgesia—Ehrlich (1952) discusses analgesia after ano-rectal surgery, when an oil-soluble anaesthetic has been used. The author states that Intracaine in oil is a compound which has a higher anaesthetic index than that of procaine and produces longer, quicker and more uniform anaesthesia. He gives an analysis of the results of this oil-soluble anaesthetic agent in 540 cases of ano-rectal surgery. There is a marked decrease in post-operative pain in proctological surgery after the use of these oil-soluble anaesthetics. Intracaine in oil is free from side-effects and neither sloughing nor abscess occurred in the author's cases. A 5 per cent solution was adopted by him in these cases. The degree of anaesthesia and duration could only be estimated. In the author's cases the majority of patients were comfortable during their period as in-patients, which lasted from 4 to 5 days. From the fifth post-operative day onwards the degree of analgesia gradually declined.

Ehrlich, R (1952) *Amer. J. Surg*, 83, 185.
Ripstein, C B (1952) *Amer. J. Surg.*, 83, 68.

SPINAL COLUMN

See also B.S.P., Vol. 7, p. 539, S Key 306.

Thoracic spine

Complete dislocation

[illegible] Wright and Gardner (1952) describe a case of bilateral [illegible] ic spine A male patient [illegible] had [illegible] location of the sixth thor [illegible] in both pleural cavities. [illegible] assumed that a sudden flow of chyle took place immediately before death, possibly [illegible] by (1) haemoconcentration, (2) ingestion of fluid and food, (3) anoxia, and (4) increased venous pressure.

Injuries of the spine

Fracture-dislocation

Clinical picture.—An unusual case of fracture-dislocation of the spine is described by Winston (1952). The patient complained of pain in the back and of "pins and needles" in

A plaster jacket was applied after 2 weeks, and a spinal brace at 3 months, when examination showed improved muscle power but residual impairment of sensation.

Winston, M. E. (1952). *J. Bone Jt Surg*, 34B, 88.
Wright, P. R., and Gardner, A. M. N (1952) *J. Bone Jt Surg.*, 34B, 64

SPLEEN—SURGERY OF

See also B S P., Vol 8, p. 1, S Key 308.

Radiological diagnosis

Visualization of splenic and portal circulation

can be examined, and the site of the obstruction demonstrated, before operation The patient is placed supine on an x-ray table and, with the breath held, 20 millilitres of 70 per cent Diodrast, heated to body temperature, are injected rapidly into the spleen using a small

vein.

Malignant tumour of the spleen

Banti's syndrome

Diagnosis

Decision as to splenectomy.—MACKEY (1952) discusses the pre-operative and post-operative aspects of splenectomy in Banti's syndrome The essential elements in Banti's syndrome are *anaemia and splenomegaly, due to obstruction of the venous return from the spleen* In some cases a major factor in the anaemia is the occurrence of repeated haematemesis or melaena. In others episodes of gross bleeding do not occur, and it appears that the anaemia is directly due to the action of the spleen itself, exerted either in an immediately destructive

of blood transfusion; in some of the diseases concerned, however, especially acquired haemolytic anaemia, such transfusion may be poorly tolerated. Splenectomy, in most circumstances, is one of the simpler surgical operations. The author points out that the responsibility for the decision as to whether or not it should be carried out must, in large measure, be borne by the physician, and more specifically by the haematologist.

Essential thrombocytopenic purpura

Acute fulminating phase

Treatment by splenectomy.—GIANNINI (1952) reviews the literature on acute essential thrombocytopenic purpura, with particular regard to the severe fulminating episode, and reports on 9 cases in the acute fulminating phase which were treated by splenectomy. The age of these patients varied from 13 to 67 years with a ratio of 2 females to every male. All the cases appeared toxic and showed a pre-operative low-grade pyrexia which disappeared after recovery from the splenectomy. Pre-operative platelet counts varied from nil to 60,000 per cubic millimetre; post-operatively an ultimate rise in the platelet count to near normal levels occurred, in most cases startin[illegible] simultaneously with the subsidence of [illegible] in 5 cases and all showed delayed or [illegible] and back occurred in 5 of the cases [illegible] the slower method of clamping the splenic vessels first. In 3 cases accessory spleens were found and removed. Gross and microscopical examination of the excised spleens showed inconclusive findings of (1) perisplenitis, (2) hyalinization of fibrous septa and capsule, (3) hyperplasia of the reticulo-endothelial system, (4) congestion of the splenic sinuses, and (5) increased number of eosinophils in the splenic red pulp. Total leucocyte counts showed consistently a post-operative temporary rise to 20,000–30,000. Splenectomy as a life-saving procedure was successful in all these cases, and has been successful in preventing recurrences in 7 out of the 9 cases.

Splenectomy

Indications and technique

Operative mortality—The indications and technique of splenectomy are discussed by MAINGOT (1952) The results depend largely on selection of cases by the haematologist. Splenectomy is indicated as an adjunct to other surgery, in ptosis and in rupture of the spleen, in congenital haemolytic anaemia, in idiopathic primary purpura haemorrhagica, splenic neutropenia and panhaematocytopenia, and in cysts and primary tumours of the spleen It may be indicated in congenital splenomegaly (portal hypertension), acquired haemolytic anaemia, secondary purpura haemorrhagica and panhaematocytopenia, lym- [illegible] ...ly (schisto- [illegible] spleens, if [illegible] ...ian, trans- [illegible] ...ndicated in portal hypertension. Cases of ptosis, primary purpura and splenic neutropenia, congenital haemolytic anaemia, panhaematocytopenia, and cysts show a low operative mortality and excellent late results, hypersplenism and many cytopenias of *known* origin have also a low mortality but show disappointing late results. Splenectomy should be combined with splenorenal or porta-caval anastomosis in most cases or portal hypertension; the high operative mortality is attributable to the nature of the disease, faulty selection of cases, and imperfections in technique The results, in experienced hands, have been promising in selected cases

[illegible] ...spleen is [illegible] ...it makes [illegible] into the [illegible]

... specific and definite

or sickled, this rule applying also to acquired ...
splenectomy, in the author's experience, have all shown the paradox of an apparent aplastic anaemia, as judged by the peripheral blood, and a definite normoblastic hyperplasia of the ... Splenectomy is also recommended in many cases of unexplained refractory ...

... 's

a risk when performed ... formed with confidence if the circulating platelets are grossly reduced, and if the marrow shows a normal or excessive number of megakaryocytes.

... (1952) *Lancet*, 1, 530.
229.

1, 990

STOMACH—DISEASE OF

See also B S P., Vol. 8, p 49, S Key 312.

Tumours

Surgical methods

Thoracico-abdominal incision —BEAL and LONGMIRE (1952) describe the use of the thoracico-abdominal incision for approaching large neoplasms arising in the upper abdomen. An ... right rectus muscle to a ...

closure. The diaphragm is incised towards the oesophageal hiatus, the lower lobe of the left lung being carefully retracted, a rib-spreading retractor is inserted and gradually extended during the incision. The method has been used in operations on 10 male patients and 1 ... from 26 to 72 years. The cases included 7 of carcinoma of ...

the pancreas when gastrectomy is performed for carcinoma of the stomach The technique described permits of extraperitoneal exploration and inspection of the coeliac and aortic lymphatic glands without division of any important structure, and the more adequate exposure facilitates extensive regional resection.

Carcinoma

Clinical history

Laparotomy was performed in 63 per cent of cases and resection of the growth in 30 per cent. With regard to end-results, 4 out of 5 patients in the whole series were dead within 1 year of admission and 19
were alive after 5
of the history. Th
did not explain this finding, and the authors conclude that it was due to the occurrence of slow-growing carcinomas.

Sarcoma of the stomach

Lymphosarcoma

Diagnosis and treatment.—CRILE, HAZARD and ALLEN (1952) present an analysis of 19 cases of primary lymphosarcoma of the stomach. The ages of the patients ranged from 31 to 78 years; the ratio of males to females was 2 : 1. The cases resembled carcinoma of the stomach so closely, clinically, that only one was diagnosed correctly prior to operation. The duration of symptoms averaged 26 months; 6 patients had palpable tumours, 3 of which were tender. A diagnosis of lymphosarcoma was made by the radiologist in only 1 case. Gastroscopy, performed in 8 cases, demonstrated a tumour in every instance, but only 1 growth was

Diagnosis

Results of treatment.—TURCOT (1952) discusses sarcoma of the stomach on the basis of a series of 363 cases of malignant tumours of the stomach, diagnosed during a period of 6½ years, which contained 6 cases of sarcoma, a ratio of 1.68 per cent. Of these patients 4 were males and 2 were females, their ages ranging from 45 to 68 years. Intervals from appearance of symptoms to consultation varied from 4 months to 1 year. The most prominent symptom was epigastric pain in all cases, the next major symptom being haemorrhage; a tumour was palpable in the epigastrium in 4 cases. Radiography showed a large tumour in 5 cases; in no
the
aled
cus
was
ular
ms

and died after 5½ months; cases
data in the present series differ little from published findings; the average age, 56 years, is
rarely recorded.

Beal, J. M., and Longmire, W. P., Jun. (1952). *Arch. Surg., Chicago*, 64, 609.
Crile, G., Jun., Hazard, J. B., and Allen, K. L. (1952). *Ann. Surg.*, 135, 39.
Swynnerton, B. F., and Truelove, S. C. (1952). *Brit. med. J.*, 1, 287.
Turcot, J. (1952). *Canad. med. Ass. J.*, 66, 252.

SURGICAL TECHNIQUE

See also B.S.P., Vol. 8, p. 124, S. Key 316.

Use of cortisone and ACTH

CTH and cortisone
treatment enables
ion, and those with
t on wound healing
and the formation of granulation tissue in man vary, but it is probable that quite large doses of ACTH or cortisone are necessary to cause a delay in the production of granulation tissue
be undesirable in some in-
anulation-tissue formation
round severed tendons or

Baxter, H , Schiller, C., Whiteside, J. H , and Randall, R. E. (1952) *Amer J. Surg*, 83, 374.

THORACIC AND INTRATHORACIC INJURIES

See also B.S.P., Vol. 8, p 203, S Key 323

Injuries to the parietes

f reuniting fixing the made near the divided ends of the rib. The corners of the distal end of the rib are removed with a small rongeur and the outer and inner cortex of this rib end become a double tenon. The marrow of both ends is hollowed out and, after a double silk ligature has been threaded through the drill holes, the outer tenon is thrust into the marrow cavity of the rib stump while the lower tenon slips below its lower cortex The ligatures are then tightened. The reconstructed thoracic cage is as firm and yet as mobile as a normal cage, and presents an almost normal appearance. There is a notable lack of callus formation and bridging.

Overholt, R. H , and Kenny, L J. (1952) *Surg. Gynec Obstet.*, 94, 365

THYMUS GLAND

See also B S P., Vol. 8, p 243, S. Key 325.

Tumours

Diagnosis

Radiographic procedures—JAUNDRELL-THOMPSON (1952) reports on radiography of the thymus gland and of thymic tumours. The gland serves a dual purpose, being both a lymphatic

may be that of an apparently widened mediastinum, or of a somewhat triangular shadow projecting from the mediastinum into the lung field, usually on the right side. In older children and adults the gland is not normally demonstrable, but it may become so if pathological. In myasthenia gravis, a condition characterized by muscular debility, demonstrable thymic tumours are sometimes present The majority of thymic tumours appear to be more or less centrally placed in the anterior mediastinum, but some may be situated several centimetres to one side of the median plane, suggesting that the lobe of the thymus gland on that side is affected The author describes a diagnostic technique which he has found very successful, consisting in screening, tomograms and various radiographic projections

Jaundrell-Thompson, F (1952) *Radiography*, 18, 30

UTERUS—CERVIX AND VAGINA

See also B.S P., Vol. 8, p. 451, S. Key 341.

Cervix

Carcinoma

Treatment: panhysterectomy—BRUNSCHWIG (1952) considers radical panhysterectomy, with pelvic-node excision and a wide vaginal cuff to be the most effective operation for cervical carcinoma. There is little risk in experienced hands, the primary surgical mortality being only 0·5 per cent The pelvis is exposed through a low mid-abdominal incision: the

sigmoi
the po
well a
of the
haemo
placed in the pelvis, principally over the region of the hypogastric veins. A soft rubber drain is inserted near each ureter and brought out at the bottom of the midline incision. The

operation. Post-operatively for 2 or 3 days, fluid and electrolyte requirements are supplied by intravenous infusions only. Unless there is great oozing of blood, the pelvic pack is removed on the day after the operation under pentothal sodium anaesthesia. The patient is allowed to get out of bed on the second or third post-operative day.

Brunschwig, A. (1952). *Mod. Med. Canad.*, 7, 43.

VASCULAR SURGERY

See also B.S.P., Vol. 8, p. 489, S. Key 343.

Mitral-valve disease

Valvulotomy

Clinical assessment for operation.—Mitral-valve disease, in the light of surgical treatment, is discussed by BOURNE (1952). The clinical assessment of cases for valvulotomy necessitates

... rate and white-cell count,

Patent ductus arteriosus

Diagnosis

... (1952) stress the value of cardiac cath-

... racter, location

... bed and the electrocardiographic ... dings given. All

ventricular and pulmonary-artery hypertension. The

In 1 case the catheter passed through the defect, in

In another case an enormous patent ductus was

a thrill persisted, which was

patient with mild or moderate

shunt may be present without

pulmonary hypertension had

large shunts.

Treatment

year. If the vessel is large, short and exhibits arteriosclerotic changes, operation is regarded as unwise or at least difficult. Hence, when symptoms are noted in adults between 30 and 50 years of age, intervention may be thought too hazardous It is pointed out that with modern treatment the risks of infective endocarditis are much reduced In practice few patients refuse operation when its nature is explained A left postero-lateral thoracotomy is the standard approach, and when the ligatures are tied around the vessel the vagus and recurrent laryngeal nerve must first be demonstrated Recovery is usually uneventful, and the oxygen tent, although it should be available after operation, is rarely essential. The authors use simple ligation with 2 silk threads, and find this procedure easier than others described. Out of 82 cases only 2 were lost at operation, but 1 patient died from complications later, being handicapped by a large septal defect. Some cases showed associated pulmonary hypertension, this being a well-known association of unknown causation. Some patients had sustained damage to the recurrent laryngeal nerve before operation. A rise in aortic diastolic and systolic pressure of 10–20 millimetres was usual after recovery, while the pulmonary-artery pressures fell to about the same degree.

Adams, F. H , Diehl, A., Jorgens, J., and Veasy, L. G (1952) *J Pediat*, 40, 49.
Bourne, G. (1952). *Brit med. J.*, 1, 896
Robb, D., and Nicks, R. (1952) *N.Z med. J.*, 51, 31.

NOTER-UP, 1953

The Key Numbers in the margins correspond to those in the main volumes, in which they appear at the top left-hand corner of each right-hand page

Vol. 1

KEY NO.

1 **ABDOMINAL EMERGENCIES**

Abstracts

Intestinal rupture following non-penetrating injury [1951], p 269
Perforation of the rectum [1951], p. 269
Primary inflammation of the appendices epiploicae [1951], p. 269

2 **ABDOMINAL PAIN**

Abstract

Mesenteric cyst : aetiology and treatment [1951], p. 270

3 **ABDOMINAL WALL**

No further references

4 **ABORTION**

No further references

5 **ABSCESS**

No further references

6 **ACHLORHYDRIA AND APPETITE**

No further references

7 **ACIDOSIS**

Article

Fluid and electrolyte balance [1953], p 91
- Introduction [1953], p 91
- Applied physiology of body fluids [1953], p. 91
  - Relationship between body water and fat [1953], p 91
  - The content and distribution of body water [1953], p 92
  - Renal regulation of electrolyte and water [1953], p 94
    - Sodium [1953], p 94
    - Potassium [1953], p. 94
    - Water [1953], p 95
  - Extrarenal water losses [1953], p 95
    - Insensible water loss [1953], p 95
    - Faeces [1953], p. 95
  - Metabolism in fasting [1953], p 96
    - Deprivation of water and food [1953], p. 96
    - Deprivation of food, water being supplied [1953], p. 96
    - Deprivation of food, water and glucose being supplied [1953], p. 96
  - [illegible] [1953], p 96

[illegible]

[illegible] [1953], p. 98

[illegible]

- Clinical features of potassium deficiency [1953], p. 100
- Diagnosis of potassium deficiency [1953], p 101

Vol. 1

KEY NO.

Vol. 1

KEY NO.

7 ACIDOSIS (*cont.*):

Fluid and electrolyte balance (*cont.*):
Treatment of fluid and electrolyte disturbances (*cont.*):
Plasma substitutes (*cont.*):
Gum acacia [1953], p. 128
Gelatin [1953], p. 128
Polyvinylpyrrolidone (PVP) [1953], p. 129
Dextran [1953], p. 129
Provision of water [1953], p. 131
Replacement and maintenance of electrolytes [1953], p. 132
Isotonic saline [1953], p 132
Saline lactate [1953], p 132
Darrow's solution [1953], p. 132
The maintenance of nutrition [1953], p. 133
Jejunostomy [1953], p. 134

8 ACTINOMYCOSIS

Abstracts
Facial and cervical treatment [1953], p. 273
Pulmonary· treatment [1953], p 273

9 ADHESIONS AND CICATRICIAL STENOSES

No further references

10 ADHESIONS (PLEURAL) IN PULMONARY TUBERCULOSIS

No further references

11 ADIPOSITY

No further references

12 ADRENAL GLANDS

Article
Phaeochromocytoma [1951], p. 1

Abstracts
Phaeochromocytoma bilateral case and new diagnostic tests [1951], p. 270
Endocrine effects of the adrenal glands [1952], p. 205
Cushing's disease: remission following adrenalectomy [1952], p. 205
Chromaffin tumour in a case of arterial hypertension [1952], p 205
Medullary and cortical tumours: diagnosis and treatment [1952], p. 206
Hypofunction and hyperactivity. hazards in anaesthesia and surgical operations [1953], p. 273
Phaeochromocytoma· adrenaline and non-adrenaline effect on the benzodioxane test [1953], p 274

13 AFTER-CARE—INTRODUCTION

No further references

14 AFTER-CARE—FOLLOW-UP

No further references

15 AFTER-CARE—METHODS AND VALUE OF MASSAGE

No further references

16 AFTER-CARE—ON RETURN HOME

No further references

17 AFTER-CARE—POST-OPERATIVE

Abstract
Pain prevention: Efocaine [illegible] on [1953], p 274

Vol. 1

KEY NO.

18 AFTER-CARE—REMEDIAL AND OCCUPATIONAL THERAPY AND REHABILITATION

No further references

19 AIR PASSAGES

Article

Reconstruction of the trachea, hypopharynx and cervical oesophagus [1951], p. 193

The trachea [1951], p. 193

20 ALLERGY

Abstract

Manifestations following procaine penicillin injection [1952], p. 206

21 AMOEBIASIS—AMOEBIC INFECTION OF INTESTINE (PATHOLOGY)

No further references

22 AMOEBIASIS—AMOEBIC INFECTIONS OF INTESTINE (SURGERY)

No further references

23 AMOEBIASIS—LIVER ABSCESS AND PATHOLOGY OF AMOEBIASIS OTHER THAN INTESTINAL

Abstracts

Comparison of chloroquine and emetine treatment [1952], p. 207

Non-hepatic secondary amoebiasis: diagnosis [1952], p 207

24 AMPUTATIONS

Article

Pain—painful stumps and phantom limbs [1951], p 12

The phantom limb [1951], p. 12

Pain [1951], p. 13

Examination [1951], p. 14

Treatment [1951], p. 15

Conclusion [1951], p. 17

Abstract

Ischaemia of the leg treated by amputation [1952], p 207

25 AMYLOID INFILTRATION (AMYLOIDOSIS)

No further references

26 ANAESTHESIA—GENERAL

Critical surveys

Contributory factors in the evolution of anaesthetic technique [1952], p 127

Newer drugs [1952], p. 128

Use of electrical apparatus in surgery [1952], p 129

Advances in drug administration [1952], p 129

Muscular relaxation [1952], p 129

[illegible]

Vol. 1

KEY NO

26 ANAESTHESIA—GENERAL (*cont.*):

Local and regional analgesia [1952], p. 133
- Extradural block [1952], p. 134
- Spinal analgesia [1952], p. 135

Planned hypotension [1952], p. 137
- Hypotension by arteriotomy [1952], p. 138
- *Hypotension* by vasoconstrictor paralysis and posture [*1952*], p *139*
- [illegible]
- [illegible]
- [illegible]
- Hypotension and posture [1952], p. 148
- [illegible] hage [1952], p. 148

[illegible] [1952], p. 149

[illegible]

Abstracts
- Cyclopropane: effects of raised airway pressure during [1952], p. 208
- Complications of endotracheal anaesthesia; laryngeal sequelae [1952], p 208
- Relaxants: abnormal sensitivity to [1953], p. 275

27 ANAESTHESIA—LOCAL

No further references

28 ANAESTHESIA—REGIONAL

No further references

29 ANAESTHESIA—SPINAL

Abstract
- Results of continuous caudal analgesia in 12,000 deliveries [1951], p. 271

30 ANGINA PECTORIS

No further references

31 ANGIOMA

Abstracts
- Diathermy treatment of haemangioma and lymphangioma [1952], p 209
- Surgical removal [1952], p 209

32 ANTHRAX

Abstract
- Chloramphenicol in treatment of cutaneous anthrax [1952], p. 209

33 ANUS, ARTIFICIAL (MANAGEMENT)

No further references

34 ANXIETY STATES

No further references

35 APPENDICITIS, ACUTE

Article

Appendicitis and peritonitis [*1951*], p. 32
- Appendicitis [1951], p. 32
- General peritonitis [1951], p. 36

Abstract
- Analysis of 2,353 appendicectomies : incidence [1951], p. 271

36 APPENDIX—TUMOURS OF

No further references

Vol. 1

KEY NO.

37 ARTERIES

Article

Vol. 1

KEY NO.

Vol. 1

KEY NO

37 ARTERIES (*cont.*):

Diagnosis and treatment of acute arterial injuries [1951], p. 273
Bilateral carotid tumour [1951], p. 274
Cirsoid aneurysm of the scalp [1951], p. 274
Ligation of abdominal aorta for aneurysm [1951], p. 274
Intrasaccular endo-aneurysmorrhaphy for aneurysm of left subclavian vessels [1951], p. 275
Thrombo-angiitis obliterans of renal artery [1952], p. 210
Physiology and relief of traumatic arterial spasm [1952], p 210
Aneurysm: resection of descending thoracic aorta [1952], p 210
Dissecting aneurysm of abdominal aorta with secondary renal dysfunction [1952], p. 211

38 ARTHRITIS—SURGICAL CONSIDERATIONS

Article

Chronic arthritis [1952], p. 1
- Osteoarthritis [1952], p 1
  - Definition [1952], p. 1
  - Aetiology [1952], p. 1
  - Pathology and clinical picture [1952], p 3
  - Conservative treatment [1952], p 4
  - Surgical intervention [1952], p 6
  - Palliative operations [1952], p 6
  - Reconstructive operations [1952], p 7
- Rheumatoid arthritis [1952], p. 20
  - Comparisons with osteoarthritis and ankylosing spondylitis [1952], p 20
  - Conservative treatment [1952], p 20
  - Surgical treatment [1952], p 21

Abstracts

Aetiology of ankylosing spondylitis, role of hyaluronic acid [1951], p. 275
Acrylic splint for the hand [1952], p 211
Clinical picture and pathology of osteoarthritis [1953], p. 275

39 ARTIFICIAL LIMBS

Abstract

Preparation of stump for artificial limb leg pylons [1952], p 212

40 ARTIFICIAL PNEUMOTHORAX

No further references

41 ASEPSIS AND ANTISEPSIS

Article

Antibiotics [1951], p. 19
- Nature and history [1951], p 19
- Penicillin [1951], p. 19
- Streptomycin [1951], p. 25
- Aureomycin and chloramphenicol (Chloromycetin) [1951], p. 28
- Antibiotics from bacilli [1951], p 29

42 ASYMMETRY

No further references

43 AUTONOMIC NERVOUS SYSTEM: INTRODUCTION

Abstracts

Clinical manifestations of autonomic dysfunction [1951], p 276
Transmission of stimuli to effector organs the chemical concept [1951] p 276

Vol. 1

Vol. 2

Vol. 2

KEY NO.

56 **BLADDER—NEUROGENIC DISTURBANCES**

Abstract

Surgical techniques which give relief in painful conditions [1952], p. 213

57 **BLADDER—POUCHES**

No further references

58 **BLADDER—TUMOURS**

Abstracts

Carcinoma of the urachus [1952], p. 214
Results of treatment [1952], p. 214
Infiltrating carcinoma of the bladder: early diagnosis [1953], p 276
Results of total cystectomy for carcinoma [1953], p. 276

59 **BLINDNESS—MANAGEMENT OF**

No further references

60 **BLOOD AND BLOOD-FORMING ORGANS : BLOOD EXAMINATION**

Abstracts

Simulation of surgical conditions in sickle-cell anaemia [1951], p. 278
Coagulation: role of coagulase-globulin [1953], p 276
Thrombin conversion. prothrombin determination [1953], p 277
Blood volume and volume of erythrocytes. effect of Dextran [1953], p 277

61 **BLOOD PRESSURE : HIGH AND LOW**

Critical survey

Treatment of hypertension [1952], p 151
- General considerations [1952], p 151
- Essential hypertension [1952], p 152
  - Common sense and symptomatic treatment [1952], p. 154
  - Pyrogens [1952], p 154
  - Low salt diet [1952], p 155
  - Hexamethonium and pentamethonium salts [1952], p. 155
  - Sympathectomy [1952], p 157
  - General comment [1952], p 158
- Treatment of some diseases associated with hypertension [1952], p 158
  - Phaeochromocytoma [1952], p. 159
  - Unilateral pyelonephritis [1952], p 159

Abstracts

Surgical treatment of hypertension [1951], p 278
Surgical treatment of hypertension : adrenalectomy [1951], p 278
Pre-ganglionic sympathectomy in hypertension [1951], p 279
Results of sympathectomy in hypertension [1951], p. 279
Essential hypertension due to aberrant renal artery [1952], p. 215
Course in simple and complicated cases of hypertension [1952], p. 215
Treatment of hypertension with hexamethonium compounds [1952], p. 215
Treatment of essential hypertension by sub-total adrenalectomy [1952], p. 216

62 **BLOOD TRANSFUSION—PRACTICE**

Abstract

Complications of haemolytic reaction [1952], p 217

Vol. 2

KEY NO.

Vol. 2

KEY NO

70 BRACHIAL PLEXUS (*cont.*):

Post-operative brachial plexus paralysis (*cont.*):

Extent of the paralysis (*cont.*):

The lesser paralyses [1953], p 43

Partial paralysis [1953], p. 44

Distribution [1953], p 44

Degree [1953], p 44

Sensory dysfunction [1953], p 44

Pain [1953], p. 44

[illegible]

49

[illegible]

Injuries by compression [1953], p. 50

Direct pressure [1953], p 50

"Nipping" of plexus between clavicle and first rib [1953], p 50

Injury between clavicle and border of scalenus medius [1953], p 50

Compression between clavicle and lower cervical transverse process [1953], p 50

Summary [1953], p 50

[illegible]

Prognosis [1953], p. 58

Medico-legal aspects [1953], p 58

71 BRAIN—ABSCESS

Abstracts

Diagnosis and treatment of brain abscess occurring in relation to infection of ear, nose and throat [1951], p. 282

Treatment of otogenic brain abscess surgical techniques [1951], p. 282

Otogenic cerebellar abscess [1952], p 220

Treatment by aspiration and antibiotic replacement [1953], p 281

End-results of treatment by aspiration [1953], p 282

72 BRAIN—CONGENITAL DEFECTS

No further references

73 BRAIN—FUNGUS

No further references

74 BRAIN—INJURIES AND COMPLICATIONS

Abstracts

Radiological diagnosis of chronic subdural haematoma in early life [1951], p. 283

Pathology of blunt head injury [1951], p 283

Concussion and haemorrhage. aetiology [1952], p. 221

Mechanics of cerebral trauma [1952], p. 221

Visual disturbances [1952], p 222

Relation of injury to subsequent brain tumour and neural sclerosis [1952], p. 222

Vol. 2

KEY NO.

75 BRAIN—NEUROLOGICAL INVESTIGATION AND SPECIAL TESTS

Abstracts

- Angiography in diagnosis of brain abscess [1952], p. 223
- Carotid arteriography—error of technique [1952], p. 223
- Intracranial venography of dural sinuses [1952], p 223
- Ventriculography and encephalography: use in control of radiotherapy [1952], p. 224
- Radioactive minerals in diagnosis [1952], p. 224
- Uses of nuclear disintegration in diagnosis and treatment of brain tumour [1952], p. 224

76 BRAIN—TUMOURS AND TECHNIQUE

Critical survey

- Pre-frontal leucotomy [1952], p. 162
  - Introduction [1952], p. 162
  - Development of the operation [1952], p. 162
  - Techniques [1952], p. 162
  - Post-operative care [1952], p. 163
  - Complications [1952], p 163
  - General effects of the operation [1952], p. 164
  - Post-operative progress [1952], p 165
  - Effects in specific conditions [1952], p. 165
  - Physical indications and contra-indications [1952], p. 168
  - Psychiatric indications and contra-indications [1952], p. 168
  - Summary [1952], p. 168
  - The value of different types of operation [1952], p. 169

Abstracts

- Prefrontal leucotomy in a case of hypertension *[1951]*, p. 284
- A technique of prefrontal lobotomy [1951], p. 284
- Radioactive phosphorus in determining limits of spread of cerebral gliomas [1951], p. 285
- Incidence of tumours in idiopathic symmetrical hyperostosis of skull [1952], p 225
- Symptoms simulating meningitis [1952], p. 225
- Operative mortality: analysis of operation and necropsy findings [1952], p 225
- [illegible] operation [1952] p. 226
- [illegible]
- [illegible] stances [1953], p. 282
- [illegible] diagnosis [1953], p. 283
- [illegible]
- [illegible] and end-results [1953], p 284
- Posterior fossa dermoid cysts: aetiology [1953], p. 284

77 BREAST—CARCINOMA OF

Abstracts

- Investigations of internal mammary lymph chain in carcinoma of breast [1951], p. 285
- Hidden carcinoma of the breast: a comparison of cases [1951], p 286
- Temporary relief by testosterone in female patients [1951], p. 286
- [illegible] and hormones [1951], p. 286
- [illegible] 1951], [illegible] tumours [illegible] p. 287
- Surgical treatment operability and end-results [1953], p 284
- Medical treatment: sex hormones [1953], p. 285

Vol. 2

KEY NO.

78 BREAST—CARCINOMA OF, POST-OPERATIVE RADIOTHERAPY

No further references

79 BREAST—CHRONIC MASTITIS

Article

Innocent lumps in the breast [1951], p. 100
- Anatomy [1951], p. 100
- Fibroadenoma [1951], p. 100
- Fibroadenosis (chronic mastitis) [1951], p. 106
  - Epithelial changes [1951], p. 106
  - Cysts [1951], p. 108
  - [illegible]
  - [illegible] 127
  - Treatment [1951], p 128

80 BREAST—INFECTIONS

No further references

81 BRONCHIECTASIS

Abstracts

Sloughs of the tracheal mucosa associated with bronchiectasis [1951], p. 288

Aqueous contrast media in bronchography [1952], p. 226

Bronchography in infants and very young children [1952], p. 227

82 BURNS AND SCALDS

Articles

Treatment of burns [1952], p 38
- Introduction [1952], p. 38
- Classification [1952], p. 38
- The burn problem [1952], p 38
  - Loss of fluid [1952], p. 38
  - Replacement of fluid [1952], p 41
  - *Estimation of fluid requirement [1952], p. 42*
  - [illegible]
  - Nutritional care [1952], p. 51
  - Local care [1952], p. 51
  - The deep burn [1952], p. 55
    - Grafting [1952], p. 56
    - Homografts [1952], p 56
    - Infected burns [1952], p. 57
  - Present-day position [1952], p 58

Flash burns [1951], p. 132
- Definitions and introduction [1951], p 132
- Aetiology [1951], p 132
- Pathology [1951], p. 133
- Symptoms and clinical course [1951], p. 134
- Treatment [1951], p 136
- Complications [1951], p. 141

Vol. 2

KEY NO.

Vol. 3

Vol. 3

KEY NO.

85 **CAROTID BODY** (*cont.*):

The syndrome of the carotoid sinus (*cont.*):

Clinical features (*cont.*):

[illegible]

Preventive measures [1953], p. 65

Sedation [1953], p. 65

Surgical treatment [1953], p. 66

Indications [1953], p. 66

Anaesthesia [1953], p 66

Position of patient [1953], p. 66

Technique [1953], p. 66

After-treatment [1953], p 67

Results [1953], p. 69

86 **CELLULITIS, LYMPHANGITIS, ERYSIPELAS**

No further references

87 **CELLULITIS—PELVIC**

No further references

88 **CERVICAL RIB AND THE SCALENUS SYNDROME**

No further references

89 **CHEMICAL WARFARE—SURGICAL ASPECTS OF**

No further references

90 **CHEMOTHERAPY**

Critical survey

The chemotherapy of malignant diseases [1953], p 256

Introduction [1953], p 256

Endocrine therapy of prostatic and mammary cancer [1953], p. 256

Cancer of the prostate [1953], p 256

Results and side-effects [1953], p 257

[illegible] it

[1953], p. 258

Cancer of the breast [1953], p. 258

Oestrogen therapy [1953], p. 258

Androgen therapy [1953], p. 259

Side-effects of androgen treatment [1953], p. 259

Endocrine therapy of tumours other than those of the prostate and breast [1953], p. 260

Hormonal treatment of haemopoietic disorders [1953], p. 260

Cortisone ACTH in leukaemia and allied diseases [1953], p. 260

Vol. 3

KEY NO.

90 CHEMOTHERAPY (*cont.*):

Bronchogenic carcinoma [1953], p 262
Side-effects of nitrogen mustard therapy [1953], p. 262
Triethylenemelamine [1953], p. 263
1 : 4-Dimethanesulphonoxybutane (Myleran) in the treatment of chronic myelogenous leukaemia [1953], p. 265
Urethane in leukaemia and allied conditions [1953], p 265
Administration [1953], p 267
Side-effects [1953], p 268
Treatment of multiple myeloma [1953], p. 268
Antagonists of folic acid and of the "citrovorum" factor in the treatment of acute leukaemia [1953], p. 268
The clinical use of radioactive isotopes [1953], p 269

91 CHORDOMA

Abstracts
Sacro-coccygeal chordoma and chordoma in other areas [1951], p 288
Thoracic chordomas [1952], p. 230

92 CICATRICES, INCLUDING KELOID

No further references

93 CIRCUMCISION

No further references

94 CISTERNAL PUNCTURE

No further references

95 COAGULANTS AND ANTICOAGULANTS

Critical survey
Introduction [1951], p. 219
Coagulation [1951], p. 220
Estimations of clotting time [1951], p. 220
Coagulation time [1951], p. 221
Prothrombin titre [1951], p. 221
Prevention of coagulation [1951], p. 222
Clinical use of anticoagulants [1951], p. 224
Complications of anticoagulant therapy [1951], p. 227
Clinical use of coagulants [1951], p 228

Abstracts
Human fibrin foam and thrombin solution [1951], p. 289
Oxycel in the treatment of bleeding wounds [1951], p. 289
Haemorrhage following use of Tromexan [1952], p 231
Experiments with dicoumarol [1952], p. 231

96 COLIC

No further references

97 COLITIS

Abstracts
Ileostomy in ulcerative colitis [1951], p. 290
Treatment of polypoid lesions of the colon by fulguration [1951], p. 290

Vol. 3

KEY NO

Vol. 3

KEY NO.

KEY NO.

117 EAR—OTITIS MEDIA, ACUTE MASTOIDITIS

No further references

118 EAR—OTITIS MEDIA, CHRONIC CATARRHAL

No further references

119 EAR—OTITIS MEDIA, CHRONIC SUPPURATIVE

No further references

120 EAR—OTITIS MEDIA, EXUDATIVE

No further references

121 EAR—OTOSCLEROSIS

Abstracts

Haemostasis during fenestration operations [1951], p. 296
Results of fenestration operations [1951], p. 296
Some difficulties arising with fenestration operation [1952], p. 236

122 EFFUSIONS

No further references

123 ELECTRICAL REACTIONS OF MUSCLE AND NERVE

No further references

124 ELECTROCARDIOGRAPHY IN SURGICAL PROGNOSIS

No further references

125 ELEPHANTIASIS

No further references

126 EMBOLISM—AIR, PATHOLOGY

No further references

127 EMBOLISM—FAT, PATHOLOGY

No further references

128 EMBOLISM—AIR AND FAT, CLINICAL ASPECT

No further references

129 EMPHYSEMA—SURGICAL

No further references

130 ENDOMETRIOSIS

No further references

131 ENDOSCOPY—BRONCHOSCOPY

Abstract

Diagnosis of foreign bodies [1951], p. 297

132 ENDOSCOPY—CYSTOSCOPY

No further references

133 ENDOSCOPY—GASTROSCOPY

No further references

134 ENDOSCOPY—OESOPHAGOSCOPY

No further references

135 ENDOSCOPY—PERITONEOSCOPY

No further references

Vol. 3

KEY NO.

136 ENDOSCOPY—SIGMOIDOSCOPY

No further references

137 ENDOSCOPY—URETHROSCOPY

No further references

138 EPIPHYSES—DISEASES OF

No further references

139 EYE—CONGENITAL ABNORMALITIES : HEREDITY IN RELATION TO EYE DISEASE

Abstract

The clinical status of the contact lens [1951], p 297

140 EYE—EXAMINATION OF, IN SURGICAL DIAGNOSIS

No further references

141 EYE—INJURIES : NON-INDUSTRIAL, INDUSTRIAL, WAR

No further references

142 EYE IN RELATION TO ENDOCRINE DISTURBANCE

Article

- Malignant exophthalmos [1952], p 60
  - Introduction [1952], p 60
  - Classification [1952], p. 60
  - Clinical features and course [1952], p 62
  - Aetiology [1952], p. 65
  - Pathology [1952], p 65
  - Treatment [1952], p 65
- Benign exophthalmos without ophthalmoplegia [1952], p. 67
  - Simple exophthalmos [1952], 67
  - [illegible]
  - Myasthenic exophthalmos [1952], p. 70

143 EYE—THERAPEUTICS OF

No further references

144 EYE—TROPICAL AND NUTRITIONAL DISEASE

No further references

145 EYE—TUBERCULOSIS

No further references

146 EYELIDS

No further references

Vol. 4

147 FACIAL PALSY

Abstracts

- Traumatic palsy : indications and technique for surgical treatment [1951] p. 298
- Traumatic palsy : [illegible]

Vol. 4

KEY NO.

148 FACIO-MAXILLARY INJURIES AND DEFORMITIES

Abstracts

Fractures of the maxillae : diagnosis and treatment *[1951], p. 298*
Dental aspects of treatment of clefts and perforations of the palate [1951], p. 299
Operative technique for cleft lip *[1951], p. 299*
Operative technique for cleft palate and hare-lip [1951], *p. 300*
Surgical treatment of hare-lip with double cleft and displaced pre-maxilla *[1951], p. 300*
Transparotid resection of lower jaw for tumours [1951], p. 301

149 FALLOPIAN TUBES

Abstract

Primary carcinoma. aetiology and treatment [1953], p. 292

150 FASCIAL GRAFTS

Abstract

Suspension of the ptosed kidney by means of a fascia lata graft [1951], p. 103

151 FAT NECROSIS

No further references

152 FIBROSITIS

No further references

153 FILARIASIS

No further references

154 FISTULA IN ANO

Abstract

Surgical anatomy of the ischiorectal space [1951], p. 302

155 FOCAL EPILEPSY

No further references

156 FOOT—SURGERY OF

Abstracts

Morton's metatarsalgia : clinical features and treatment [1951], p. 302
Metatarsus varus : classification and treatment [1951], p. 303
Hallux valgus and hallux rigidus: treatment [1953], p. 292
Flat foot: end-result of surgical treatment [1953], p. 293
Club-foot: treatment [1953], p. 293

157, 158, 159 FRACTURES, DISLOCATIONS, FRACTURE-DISLOCATIONS AND ALLIED INJURIES

Article

[illegible]

[illegible] 192
Fractures of the anterior part of the ring [illegible], p. 192
Subluxation of the sacro-iliac joint [1953], p. 192
Disruption of the pelvic ring [1953], p. 193

Vol. 4

KEY NO.

157, 158, 159 FRACTURES, DISLOCATIONS, FRACTURE-DISLOCATIONS AND ALLIED INJURIES (*cont*):

Fractures of the pelvis (*cont.*):
- Fractures and dislocations of the pelvic ring (*cont.*):
  - Disruption of the pelvic ring (*cont.*):
    - Methods of reduction and immobilization [1953], p. 194
      - The method of lateral recumbency [1953], p. 194
      - Manipulation and pelvic sling [1953], p. 197
    - Complications [1953], p. 198
      - Injury to the bladder and urethra [1953], p. 198
      - Retroperitoneal bleeding [1953], p. 198
      - Sacro-iliac and pubic pain [1953], p. 198
- Fracture of the sacrum [1953], p. 200
- Fracture of the coccyx [1953], p. 200
- Fracture of the acetabulum [1953], p 200
  - Treatment [1953], p. 200
  - Prognosis [1953], p 201

Abstracts

Transplant of the musculospiral nerve in the open reduction of fractures of the humerus [1951], p 303
Aspiration of elbow joint following fractures of the radial head [1951], p. 303
Intramedullary pins in the treatment of forearm fractures [1951], p. 304
Bone grafting in non-union of fractures of the carpal scaphoid [1951], p 304
Treatment of adduction fractures of the neck of the femur [1951], p. 305
Treatment of fractures of the long bones by use of a medullary nail [1951], p. 305
Treatment of fractures of the neck of the astragalus [1951], p. 305
Treatment [1952], p. 236

160 FROST-BITE

Abstract

Surgical treatment end-results of sympathectomy [1953], p 293

161 GALL-BLADDER AND BILE PASSAGES

Abstracts

A case of double gall-bladder [1951], p. 306
Early operation in cases of gall-stones [1951], p. 306
Gall-bladder paracentesis by a transparieto-hepatic approach [1951], p 307
Repair of injuries: recurrent stricture [1952], p 237
Post-operative use of split T-tube [1952], p 237
Biliary tract disorders: surgical treatment [1953], p. 294
[illegible]

162 GANGLION

No further references

163 GANGRENE, CLOSTRIDIAL (GAS GANGRENE)

No further references

Vol. 4

KEY NO.

164 GASTRO-COLIC FISTULA

Abstract

Gastro-jejuno-colic fistula : a report on two cases [1951], p. 307

165 GASTROSTOMY

No further references

166 GENITAL ORGANS—FEMALE EXTERNAL

No further references

167 GLAND-PUNCTURE AND ASPIRATION BIOPSY

No further references

168 GLANDERS

No further references

169 GLAUCOMA

Abstracts

Pathogenesis . aqueous veins [1951], p. 308
Surgical relief of glaucoma [1951], p. 308
Glaucoma associated with polycystic disease of the kidney [1952], p 237
Glaucoma secondary to uveitis: cortisone treatment [1952], p. 238

170 GLOMUS TUMOURS

No further references

171 GLOTTIS—OEDEMA OF

No further references

172 GONORRHOEA

Abstract

Antibiotic treatment in the female [1952], p. 238

173 GOUT

No further references

174 GUNSHOT WOUNDS AND ALLIED INJURIES (GENERAL MANAGEMENT)

No further references

175 HAEMATOMA

Abstracts

Haematoma of the umbilical cord [1951], p. 309
Extradural haematoma [1952], p. 238

176 HAEMOPHILIA AND OTHER HAEMORRHAGIC STATES

No further references

177 HAEMORRHAGE

Abstracts

Upper gastro-intestinal haemorrhage [1952], p. 239
Idiopathic thrombopenic purpura: effects of ACTH and cortisone on the platelet count [1953], p. 296

Vol. 4

KEY NO.

178 HAND

Critical surveys
- Infections [1951], p. 231
- Trauma [1951], p. 233

Abstract
- Reconstruction of the thumb: choice of method [1953], p. 296

179 HEART AND PERICARDIUM

Article
- Chronic constrictive pericarditis [1953], p. 87
  - Definition [1953], p 87
  - Aetiology [1953], p 87
  - Pathology [1953], p. 87
  - Clinical picture [1953], p. 87
  - Special aids to diagnosis [1953], p. 88
    - Cardiac catheterization [1953], p 88
  - Differential diagnosis [1953], p 88
  - Surgical treatment [1953], p 88
    - Indications [1953], p 88
      - Age considerations [1953], p. 88
      - Pericardiectomy in tuberculous pericarditis [1953], p. 88
      - Pericardiectomy in the presence of bilateral constrictive pleuritis [1953], p 89
    - Technique [1953], p 89
      - Median sternotomy [1953], p 89
  - Results of treatment [1953], p 90

Abstracts
- Deaths due to cardiac injury during intrathoracic surgery [1951], p. 309
- Post-operative changes in output [1952], p. 239

180 HERNIA

Article
- Recurrent hernia [1951], p 146
  - Incidence of recurrence [1951], p. 146
  - Interval between operation and recurrence [1951], p. 147
  - Causes of failure after operation [1951], p 147
  - Indirect inguinal hernia [1951], p 153
  - Direct inguinal hernia [1951], p 159
  - Femoral hernia [1951], p. 160
  - Operations for umbilical hernia [1951], p 161
  - Incisional hernia [1951], p 161

Abstracts
- Anatomy of inguinal hernias [1951], p. 310
- Surgical treatment of inguinal hernia [1951], p 310
- [illegible]
- [illegible] p. 312
- Sliding hernia of the colon : trans-abdominal operation [1951], p. 312
- Whole-thickness skin grafts in treatment [1951], p. 312
- Hernias in aged people [1951], p. 313
- Recurrent inguinal hernia: skin-grafting at operation [1952], p 240
- Oesophageal hiatus hernia: operative procedure [1953], p. 297

Vol. 4

KEY NO.

181 HERNIA—DIAPHRAGMATIC

Abstracts

Traumatic hernias of the diaphragm [1951], p. 313
Differential diagnosis from coronary artery disease [1951], p. 314

182 HERPES ZOSTER

No further references

183 HETEROTOPIA

No further references

184 HICCUP

No further references

Vol. 5

185 HODGKIN'S DISEASE, OTHER RETICULOSES, RETICULO-SARCOMA AND MYELOMATOSIS

No further references

186 HORMONES

No further references

187 HYDATID DISEASE

Abstract

Operative removal of univesicular pulmonary hydatid cyst [1951], p 314

188 HYPERHIDROSIS AND ALLIED STATES

No further references

189 HYPERPIESIA

No further references

190 IMMERSION-FOOT

No further references

191 IMPOTENCE

No further references

192 INFECTION, INFECTIONS AND INFLAMMATION

No further references

193 INJURY—CIVIL AND INDUSTRIAL

No further references

194 INJURY—COMPRESSION

No further references

195–199 INTESTINES

Critical survey

Vol. 5

KEY NO.

195–199 INTESTINES (*cont.*):

Regional ileitis [1952], p. 173
Neoplasms of the small intestine [1952], p. 174
Intestinal obstruction [1952], p. 175
[illegible]
X-ray appearances [1952], p 178
Varieties of intestinal obstruction [1952], p. 178
Intestinal obstruction due to food [1952], p. 178
Gall-stone obstruction [1952], p. 178
[illegible] [1952], p. 179
[illegible]
Mesenteric vascular occlusion [1952], p 180
Inferior mesenteric arterial occlusion [1952], p. 182
Intestinal volvulus [1952], p 182
Volvulus of the caecum [1952], p. 182
Acute intussusception [1952], p. 183
Intussusception in adults [1952], p 185

Abstracts

Survey of literature and report on 34 cases of Crohn's disease [1951], p. 315
Multiple argentaffinomas of the ileum [1952], p. 240
Argentaffinoma of ileum with perforation [1952], p 240
Congenital duodenal obstruction and mongolism [1952], p. 241
Congenital duplication of the small intestine [1952], p. 241

200 INTUSSUSCEPTION

Abstract

Intussusception associated with aberrant pancreatic tissue [1951], p. 315

201 ISCHAEMIA

No further references

202 JAUNDICE

Abstract

Intrahepatic obstructive jaundice of unknown aetiology [1952], p. 241

203 JOINTS—ARTHROGRAPHY

No further references

204 JOINTS—CAISSON DISEASE OF

No further references

205 JOINTS—INJURIES AND ACUTE INFECTIONS

No further references

206 JOINTS—INTERNAL DERANGEMENTS OF THE KNEE

No further references

207 JOINTS—TUBERCULOSIS

Abstract

Streptomycin in surgery [1952], p. 242

Vol. 5

KEY NO.

208 KIDNEY AND URETER—CYSTS

Abstracts

Polycystic disease: radical operation [1952], p. 242
Multilocular cysts [1952], p 242

209 KIDNEY AND URETER—DENERVATION OF THE KIDNEY

No further references

210 KIDNEY AND URETER—GROWTHS

Abstracts

Ureteral tumours [1951], p. 316
Aetiology, diagnosis and treatment of Wilms' tumour [1951], p. 316
Haemangioma: clinical picture [1952], p. 243
Thrombosis of vena cava associated with renal neoplasia [1952], p. 244
Retrocaval displacement [1952], p. 244
Transthoracic nephrectomy [1952], p. 244
Malignant tumours: symptoms, diagnosis and treatment [1953], p 297
Late metastasis from renal carcinoma [1953], p. 297

211 KIDNEY AND URETER—HYDRONEPHROSIS AND PYONEPHROSIS

Abstracts

Transparietal puncture of the renal pelvis [1951], p. 317
Plastic repair of retrocaval ureter [1951], p. 317

212 KIDNEY AND URETER—STONE

Abstract

Incidence of vesical calculus in Norfolk [1951], p. 318

213 KIDNEY AND URETER—TUBERCULOSIS

No further references

214 LACRIMAL APPARATUS—INJURIES AND DISEASES

Abstracts

Primary adenocarcinoma of the lacrimal gland [1952], p. 245
Mixed tumour of lacrimal gland [1952], p. 245

215 LARYNX—DIRECT LARYNGOSCOPY AND ASPIRATION TREATMENT IN LARYNGEAL DIPHTHERIA

No further references

216 LARYNX—SURGICAL DISEASES OF

Abstracts

Streptomycin in the treatment of scleroma [1951], p. 318
Indications for a preliminary tracheotomy [1951], p. 318
Surgery after failure of radiotherapy for carcinoma [1952], p. 245
Emergency operations for the treatment of grave dyspnoea [1952], p 246
Malignant disease: treatment by radiotherapy [1953], p. 298

217 LAW IN RELATION TO SURGERY

No further references

218 LENS—DISEASES AND INJURIES

Abstract

Cataract: intra-ocular acrylic lenses in post-operative management [1952], p. 246

Vol. 5

KEY NO.

Vol. 5

KEY NO.

225 LUNG—TUMOURS (*cont.*):

Incidence of metastasis of lung tumours of the brain [1951], p. 320
Carcinoma of the lung: incidence [1952], p. 247
Coexistence of pulmonary tuberculosis with bronchial carcinoma [1952], p. 248
Morbid anatomy of cancer of the lung [1953], p. 298

226 LUPUS VULGARIS

Abstracts

Intralesional calciferol treatment [1952], p. 248
Lupus erythematosus: morbid anatomy [1953], p. 299

227 LYMPHOGRANULOMA INGUINALE

No further references

Vol. 6

228 MALINGERING

No further references

229 MANIPULATIVE SURGERY

No further references

230 MEDIASTINUM

Abstract

Mediastinal fascia: anatomy and applied anatomy [1953], p. 299

231 MELAENA AND BLOOD IN THE STOOLS

No further references

232 MELANOMA

Abstract

Treatment of malignant melanoma [1953], p. 300

233 MENINGES—MENINGITIS, ACUTE AND CHRONIC

Article

Surgical aspects of meningitis [1953], p. 136
Introduction [1953], p. 136
Acute pyogenic meningitis [1953], p. 136
Diagnosis [1953], p. 136
Lumbar puncture [1953], p. 138
Cerebrospinal fluid [1953], p. 139
Cells [1953], p. 139

Following operations on the cranium [1953], p. 149
Mastoidectomy [1953], p. 149
Paranasal sinus operations [1953], p. 150
Sphenoidal approach to the pituitary [1953], p. 150

Vol. 6

KEY NO.

233 MENINGES—MENINGITIS, ACUTE AND CHRONIC (*cont.*):

Vol. 6

KEY NO.

244 NOSE, NASOPHARYNX AND ACCESSORY SINUSES

Abstracts

Diagnosis and treatment of mucocele of the sinuses [1951], p. 324
Malignant tumours of the nasopharynx [1952], p. 251
Treatment of ulcerative destruction of the nose with chloramphenicol [1953], p. 301
Chondrosarcoma, clinical picture and prognosis [1953], p 302
Intranasal encephaloceles: diagnosis and treatment [1953], p 302

245 ODONTOMES AND EPITHELIAL CYSTS

Abstract

Diagnosis and treatment of maxillary cysts [1951], p 324

246 OEDEMA—TRAUMATIC

No further references

247 OESOPHAGUS

Articles

Reconstruction of the trachea, hypopharynx and cervical oesophagus [1951], p. 193
The hypopharynx and cervical oesophagus [1951], p 201
Experimental surgery [1951], p 203
The operation [1951], p. 203
Post-operative care after primary repair with a free skin graft [1951], p. 207
Conclusions [1951], p 207
Cardiospasm [1953], p 178
Aetiology [1953], p. 178
Psychological factors [1953], p. 179
[illegible] 179
[illegible]
Age considerations [1953], p 180
Hydrostatic pressure [1953], p 180
Maintenance of nutrition [1953], p 181
Dysphagia [1953], p 181
Loss of weight [1953], p 181
Regurgitation and vomiting [1953], p 182
Pulmonary symptoms [1953], p 183
Radiological appearances [1953], p 184
Oesophageal appearances [1953], p 186
Treatment [1953], p 186
[illegible] 186
[illegible]

Abstracts

[illegible]
Simple tumours of the oesophagus [1952], p 253
Treatment for accidental perforation of the oesophagus [1953], p. 302
Complications of foreign-body invasion of the oesophagus [1953], p. 303

Vol. 6

KEY NO.

248 OMENTUM

Abstracts

Diagnosis and treatment of torsion of the omentum [1951], p. 326
Torsion of great omentum: surgical treatment [1952], p. 254

249 OPTIC NERVE

No further references

250 ORBIT—INJURIES, INFECTIONS, NEOPLASMS

Abstract

Tumours of the orbit [1951], p. 327

251 ORTHODONTICS

Abstract

Trends in orthodontic treatment [1951], p. 327

252 ORTHODONTICS—SURGERY OF

No further references

253 ORTHOPTIC TRAINING

No further references

254 OVARY

Abstracts

Carcinoma: review of a series [1952], p. 254
Carcinoma: vaginal metastases [1953], p. 303

255 OXYGEN THERAPY

No further references

256 PAIN—CAUSALGIA

No further references

257 PANCREAS

Abstracts

Heterotopic pancreatic tissue [1951], p. 328
Fibrocystic disease and acute intestinal obstruction [1952], p. 255
Fibrocystic disease with meconium peritonitis [1953], p. 304
Aberrant pancreas as a cause of duodenal syndrome [1953], p. 304
Traumatic pancreatitis: causation [1953], p. 304
Treatment of annular constriction [1953], p. 305
Islet-celled tumours [1953], p. 305
Carcinoma of the ampulla of Vater: symptoms, signs and treatment [1953], p. 305
Carcinoma of the pancreas: radiological diagnosis [1953], p. 305
Carcinoma of the head of the pancreas: treatment [1953], p. 306
Total extirpation of the pancreas: end-results [1953], p. 306
Islet-celled adenoma with hyperinsulinism: treatment [1953], p. 306

258 PARALYSIS—MANAGEMENT OF

Abstracts

Transplantation of the spinal cord in paraplegia [1951], p. 328
Infantile hemiplegia treated by hemispherectomy [1952], p. 255

Vol. 6

KEY NO

259 PARATHYROID GLAND—DISEASES

Abstracts

Hyperparathyroidism : results of surgical treatment [1951], p. 329
Hyperparathyroidism: differential diagnosis from sarcoidosis [1952], p. 256

260 PELLAGRA

No further references

261 PELVIC ORGANS—DISPLACEMENT

Critical survey

Stress incontinence [1951], p. 259
 Introduction [1951], p 259
 Clinical findings [1951], p 259
 Repair of defects in the urethral supports [1951], p. 259

Abstracts

Stress incontinence in women with genital prolapse [1952], p. 256
Stress incontinence: failure of cure following vaginal operative procedure [1952], p. 256

262 PEPTIC ULCER AND ITS COMPLICATIONS

Article

Gastric ulcer: the vascular anatomy of the human stomach in relation to [1952], p. 104
 The arterial side of the vascular tree [1952], p. 104
 The venous side of the vascular tree [1952], p. 117
 The vessels of a gastric ulcer [1952], p 119

Abstracts

Causation of peptic ulceration [1951], p 330
Hormonal overaction in relation to gastric secretion in chronic duodenal ulcer [1951], p. 330
Banthine in the treatment of peptic ulcer [1951], p. 330
Medical and surgical treatment of cases of peptic ulcer with gross bleeding [1951], p 331
[illegible]
[illegible] otomy [1951], p. 332
Results of vagotomy in peptic ulcer [1951], p. 332
Partial gastrectomy for peptic ulcer [1951], p. 333
Subtotal gastric resection and bilateral vagotomy for gastric and duodenal [illegible]
[illegible]
Medical and surgical treatment in general practice [1952], p 257
Surgical treatment for duodenal ulcer [1952], p. 258
Gastric resection for duodenal ulcer [1952], p. 258
Late results of resection for gastro-duodenal ulcer [1952], p. 258
Gastrectomy: post-operative syndromes [1952], p. 259
Post-gastrectomy "dumping" syndrome [1952], p. 259
[illegible]

Subsequent stricture and cardiospasm after oesophageal ulcer [1952], p. 261

Vol. 6

KEY NO.

262 **PEPTIC ULCER AND ITS COMPLICATIONS** *(cont.)*:
Achalasia: cardiospasm [1952], p. 261
Perforations: end-results of operation [1952], p. 262
Experimental transplantation of gastric tissue in prevention [1952], p. 262
Gastro-jejunal ulceration: aetiology and treatment [1953], p. 307
Gastro-jejunal ulceration: treatment by vagotomy [1953], p. 307
Gastrectomy and colonic replacement in treatment of gastric ulcer [1953], p. 308
Gastrectomy: post-operative dumping syndrome [1953], p. 308
Treatment of perforated gastric ulcer [1953], p. 308
Gastric and duodenal: treatment [1953], p. 309

263 **PERFORATING ULCER OF THE FOOT**
No further references

264 **PERITONEUM AND PERITONITIS**
Article
Appendicitis and peritonitis [1951], p 32
General peritonitis [1951], p. 36

Vol. 7

265 **PHARYNGEAL DIVERTICULA**
Abstracts
Mechanism of herniation [1951], p. 334
Pharyngo-oesophageal diverticulosis: surgical treatment [1953], p. 309

266 **PHYSIOTHERAPY**
Abstract
Electromyography in orthopaedics [1951], p. 335

267 **PHYSIQUE, BODY BUILD AND POSTURE**
No further references

268 **PITUITARY TUMOURS**
No further references

269 **PLASTIC SURGERY—CORNEAL GRAFTING**
No further references

270–273 **PLEURA—DISEASES OF**
Critical survey
... debridement) [1953], p. 235

'40

Abstract
Pleural cysts: development and treatment [1952], p. 263

274 **POLIOMYELITIS**

Vol. 7

KEY NO

275 **POLYCYSTIC DISEASE**

Abstracts

Unilateral polycystic kidney disease [1951], p. 335
Renal lesions in the child· aetiology [1952], p 263

276 **POST-OPERATIVE GANGRENE**

No further references

277 **PREGNANCY—SURGICAL INTERVENTION DURING**

Abstracts

Indications: assessment of risks [1951], p. 336
Management of ectopic pregnancy [1953], p. 310

278 **PROSTATE**

Abstracts

[1951], p 337
Care and treatment of cases submitted to prostatectomy: use of sump drainage of the bladder [1951], p 338
Retropubic prostatectomy with preservation of prostatic urethra [1952], p. 265
Complications of prostatectomy [1952], p. 265

279 **PROTRACTED ILLNESS—MANAGEMENT AND REHABILITATION**

No further references

280 **PULMONARY ABSCESS**

No further references

281 **PULMONARY TUBERCULOSIS**

Abstracts

Streptomycin in the surgical treatment [1951], p. 338
Pneumoperitoneum treatment: indications and technique [1951], p. 339
[1953], p 311

282 **PYLEPHLEBITIS**

No further references

Vol. 7

KEY NO.

Vol. 7

KEY NO.

290 **RECTUM—CACRINOMA OF** *(cont.)*:
Vesical dysfunction following abdomino-perineal recto-sigmoidectomy [1951], p. 341
[illegible] with colostomy [1951], p 341

[illegible] operative obstruction of the

291 **RECTUM—HAEMORRHOIDS**
No further references

292 **RECTUM—PROCTITIS**
No further references

293 **RECTUM—PROLAPSE**
Abstracts
Treatment for massive prolapse [1953], p. 312
Oil-soluble anaesthetics and lasting analgesia [1953], p 312

294 **REFRIGERATION ANAESTHESIA**
No further references

295 **RESUSCITATION**
No further references

296 **RETINA**
Article
Retinal detachment: improvements in investigation and treatment [1953], p. 224
- Ophthalmoscopy [1953], p 224
  - Finding the tear [1953], p 224
    - Corneal transparency [1953], p 224
    - Mydriasis [1953], p 225
  - Methods of ophthalmoscopy [1953], p 225
    - Direct method [1953], p 225
    - Indirect method [1953], p 225
    - Trantas' method [1953], p 225
    - Combination of direct and indirect methods [1953], p 226
- The role of the vitreous in detachment of the retina [1953], p 226
  - Examination with the slit-lamp [1953], p. 226
  - Detachment of the vitreous [1953], p. 226
  - Effects of operations for cataract [1953], p 227
- The importance of the choroid [1953], p. 228
  - The choroid in spontaneous cure of retinal detachment [1953], p. 228
- Scleral resection [1953], p 228
  - *Comparison with other methods [1953], p 228*
      - Diathermal and chemical coagulation [1953], p 228
  - Development of scleral resection [1953], p 229
  - Methods of scleral resection [1953], p. 229
    - Perforating (full-thickness) scleral resection [1953], p. 229
    - Partial-penetrating (or lamellar) scleral resection [1953], p 231
  - Indications for operation [1953], p 231
      - Aphakia [1953], p 231
      - Vitreous strands and retinitis proliferans [1953], p 231

KEY NO.

296 RETINA (*cont.*):

Retinal detachment. Improvements in investigation and treatmen
Scleral resection (*cont.*):
Results of scleral resect... [illegible]

Abstract
Diathermy and antibiotics in simple detachment [1952], p. 270

297 SACRO-COCCYGEAL REGION—SURGERY OF

Abstract
Sacro-coccygeal pilonidal cyst [1951], p. 342

298 SALIVARY GLANDS

Abstracts
Functions of the parotid gland [1951], p. 342
Results of radiation therapy in parotid tumours [1951], p. 343
Repair of lacerated parotid duct [1951], p. 343

299 SCALP AND SKULL

No further references

300 SCHISTOSOMIASIS

No further references

301 SCIATICA

No further references

302 SCLERA

No further references

303 SCURVY—MASKED AND MANIFEST

No further references

304 SKIN—DISEASES OF, IN RELATION TO SURGERY

No further references

305 SPEECH THERAPY

No further references

306 SPINAL COLUMN

Article
Spondylolisthesis [1951], p. 174
Definition [1951], p. 174
Pathological anatomy [1951], p. 174
Frequency of occurrence of the defect at the isthmus which perm
spondylolisthesis to occur [1951], p. 177
Aetiology of spondylolisthesis and the relation to it of trauma [19
p. 177
Clinical manifestations of spondylolisthesis [1951], p. 179
Diagnosis [1951], p. 184
Treatment [1951], p. 184

Abstracts
Diagnosis and treatment of spinal caries (Pott's disease) [1951], p. 344
Surgical treatment of Pott's disease (spinal caries) [1951], p. 344

Vol. 7

ITEM NO

306 SPINAL COLUMN (*cont.*)

Fracture of spinous processes by muscular action operative treatment [1951], p. 345
Non-traumatic atlanto-axial dislocation causing quadriplegia [1951], p 345
Mechanism of cervical radicular lesions [1952], p 270
Compression of cervical nerve roots [1952], p. 271
Herniation of the nucleus pulposus [1952], p. 271
Cervical and upper thoracic fractures [1952], p. 271
Indications for operation on protruded discs, and results of operation [1952], p. 271
Electromyograms in cases of post-operative pain due to stretch injury [1952], p. 272
Complete dislocation of thoracic spine [1953], p 312
Fracture-dislocation: clinical picture [1953], p 312

307 SPINAL CORD

Abstracts

Diagnosis and treatment of intraspinal tumours [1951], p 346
Neurofibroma: benign, intraspinal-intrathoracic "hour-glass" tumour with paraplegia [1951], p. 346
Intramedullary abscess of the spinal cord [1951], p. 347
Surgical treatment of chronic intractable pain [1951], p. 347
Relief of pain: chordotomy, sympathectomy and prefrontal leucotomy [1951], p. 347
Compression paraplegia: rare causes and treatment by laminectomy [1952], p. 272
Lumbar and sacral cysts [1952], p. 273
Surgical treatment of pain [1952], p. 273

Vol. 8

308 SPLEEN—SURGERY OF

Abstracts

Indications for porta-caval shunt in splenic anaemia [1952], p. 274
Porta-caval, spleno-renal and other venous shunts in splenic anaemia [1952], p. 274
Kala-azar: effects and treatment by splenectomy [1952], p 274
Diagnostic radiology in visualization of splenic and portal circulation [1953], p. 313
Malignant tumour of the spleen [1953], p 313
Banti's syndrome: diagnosis [1953], p 313
Essential thrombocytopenic purpura: treatment by splenectomy [1953], p. 314
Splenectomy: indications and technique [1953], p 314
Splenectomy: anatomical and physiological considerations [1953], p 314

309–310 STERILITY AND STERILIZATION

No further references

311 STERILIZATION OF SURGICAL APPARATUS

Abstracts

Sterilization of operating-room by means of antibiotics [1951], p. 348
Bactericides: benzchlorophenol [1952], p. 275

Vol. 8

KEY NO

312 STOMACH—DISEASES OF

Abstracts

Indications for gastrectomy and for vagotomy [1951], p. 348
Gastro-intestinal lymphosarcoma [1951], p. 349
Gastric obstruction resulting from the swallowing of corrosive poison [1952], p. 275
Tumours surgical methods of treatment [1953], p. 315
Clinical history of carcinoma and results of resection [1953], p. 315

313 STRABISMUS AND HETEROPHORIA

Abstract

Esophoria surgical treatment [1952], p. 276

— STRESS INCONTINENCE, *see* Pelvic Organs

314 SUBPHRENIC ABSCESS

Abstracts

Anatomy, clinical picture, diagnosis and treatment of subphrenic abscess [1951], p. 349
Incidence and treatment of subphrenic abscess [1951], p. 350

315 SUPRASPINATUS LESIONS

No further references

316 SURGICAL TECHNIQUE

Abstracts

Control of the circulation with hypotensive drugs and by posture [1951], p 350
Fortisan as a suture material [1951], p. 351
Use of cortisone and ACTH: effect on healing [1953], p. 316

317 SURGICAL TECHNIQUE—WOUND DRESSINGS

No further references

318 SYPHILIS

No further references

319 TABES DORSALIS (LOCOMOTOR ATAXIA)

No further references

320 TESTICLE AND TUNICA VAGINALIS

Abstracts

The undescended testicle : timing of surgical treatment [1951], p. 351
Hydrocele : injection treatment [1951], p. 352
Testicular tumours : pathological study [1951], p. 352
Histology of testicular tissues and tumours and isolation of ketosteroids [1952], p. 276
Cholesteatoma of epididymis [1952], p. 277
Radiotherapy after orchidectomy [1952], p. 277
Tumours of spermatic cord · primary or secondary [1952], p. 277

321 TETANUS

No further references

Vol. 8

KEY NO.

322 TETANY

No further references

323 THORACIC AND INTRATHORACIC INJURIES

Abstracts

Studies on normal anatomy of bronchial arteries [1952], p. 278
Tantalum gauze in repair of large gunshot wound [1952], p. 278
Atelectasis: prevention and treatment [1952], p 278
Angiocardiography, intrathoracic, to display foreign bodies [1952], p. 279
Injuries to the parietes· method of reuniting ribs [1953], p 317

324 THROMBOSIS AND EMBOLISM

Abstracts

Prophylactic use of dicoumarol in pelvic and vaginal surgery [1951], p 353
Emotions in relation to clotting time and viscosity of blood [1952], p. 279
Thrombosis of renal vein in an infant [1952], p. 279
Insidious thrombosis of the abdominal aorta [1952], p. 280
Ilio-femoral thrombophlebitis: causes and treatment [1952], p 280
Aorta: embolectomy [1952], p. 280

325 THYMUS GLAND

Abstracts

Thymectomy . indications and assessment of results [1951], p 353
Radiographic procedures in diagnosis of tumours [1953], p. 317

326 THYROGLOSSAL CYST, SINUS AND FISTULA

No further references

327 THYROID GLAND—DISEASES OF

Abstracts

Medical treatment of thyrotoxicosis prior to operation [1951], p. 354
Anaesthesia in thyroid surgery · problems [1951], p. 354
Lateral aberrant cancer [1952], p 281
[illegible]

Types of thyrotoxicosis and their management [1952], p 282
Use of thiouracil in increasing uptake of radio-iodine absorption [1952], p 283
Radio-iodine in the treatment of carcinoma [1952], p. 283
Radioactive iodine as an adjunct to surgery [1952], p. 284
[illegible]

328 TONSILLITIS

No further references

329 TROPICAL DISEASE—SURGERY IN

Abstract

Treatment of ulcers [1952], p 285

Vol. 8

KEY NO.

330 TUBERCULOSIS

Abstracts

Comparative merits of measures for detecting the tubercle bacillus [1951], p. 355
The Mantoux tuberculin test in diagnosis: negative reactions [1951], p. 355
Streptomycin treatment in genito-peritoneal tuberculosis [1951], p. 355

331 TYPHOID FEVER—SURGERY IN

No further references

332 ULCERS AND ULCERATION

Abstract

Rodent ulcer of neck, trunk and limbs *[1951], p. 356*

333 UMBILICUS—DISEASES OF

No further references

334 URAEMIA

Abstracts

M[illegible] [1951], p. 356

335 URETER—TRANSPLANTATION OF

Abstracts

Pre-operative regimen and operative technique [1951], p. 358
Transplantation for bladder contracture following renal tuberculosis [1951], p. 359
Coffey uretero-enterostomy: a modification [1951], p. 359
Cordonnier's uretero-sigmoid anastomosis: technique and results [1951], p. *360*
Technique and results of extraperitoneal ureterocolic anastomosis [1951], p. *360*
Operative technique [1952], p. 287

336 URETHRA AND BLADDER—CONGENITAL MALFORMATIONS

Abstract

Hypospadias: two-stage treatment [1951], p. 360

337 URETHRA—NEW GROWTHS AND STRICTURE

Abstract

Pathogenesis and treatment of penile carcinoma *[1951], p. 361*

338 URINARY ANTISEPTICS

Abstract

Bacterial sensitivity in urinary infections [1952], p. 287

339 UTERUS—FIBROIDS

Abstracts

A technique for vaginal hysterectomy [1951], p. 361
History of Wertheim's operation *[1951]*, p. 362
Hysterectomy and abdominal colporrhaphy [1952], p. 287

Vol. 8

KEY NO.

340 UTERUS—CARCINOMA OF THE BODY

Abstracts

Diagnosis of carcinoma of the cervix uteri by sponge biopsy [1951], p. 362
Enzymatic activity in the diagnosis of uterine cancer [1951], p. 363
Comparative exfoliative cytologic diagnosis [1951], p. 363
Cytological diagnosis [1952], p. 288
Radioactive colloidal gold in localization [1952], p. 288
Prognosis in vaginal metastases [1952], p. 288

341 UTERUS—CERVIX ; AND VAGINA

Abstracts

Radium therapy of malignant lesions of the vagina [1951], p. 364
Treatment of cervical carcinoma [1953], p 317

342 UVEAL TRACT

No further references

343 VASCULAR SURGERY

Article

Surgery of the heart [1952], p 71
Congenital heart disease [1952], p. 71
Tetralogy of Fallot [1952], p. 71
Diagnosis [1952], p. 71
Choice of operation [1952], p. 72
[illegible] [1952] p 78
[illegible]
[illegible] congenital heart disease [1952], p 80
[illegible]

Investigation [1952], p. 83
Pre-operative measures [1952], p 83
Operative technique [1952], p. 84
Post-operative care [1952], p 85
Results [1952], p. 85
Aortic valvular disease [1952], p. 86

Critical survey

Chronic oedema of the leg [1952], p 188
[illegible]

[illegible] p 195
[illegible]
[illegible] *for lymphoedema* [1952], p 200
Excisional operations for lymphoedema [1952], p. 201

Vol. 8

KEY. NO

343 VASCULAR SURGERY (*cont.*):

Abstracts

Persistent hypertension due to coarctation of the aorta and its operative treatment [1951], p. 364
Aortic vascular rings encountered in congenital pulmonary stenosis [1951], p. 364
Anaesthesia for surgery of the heart and great vessels [1951], p. 365
Early operation for congenital heart disease [1951], p. 365
Congenital and acquired heart disease [1951], p 366
The cardiac lung [1951], p 366
Clinical plethysmography and the treatment of vascular disease [1951], p. 367
Regional heparinization in vascular surgery [1951], p. 367
Maintenance of life by mechanical heart and lung during occlusion of the venae cavae [1951], p. 368
Vascular grafts: viability of canine aortic transplant [1952], p. 289
Blood-vessel bank [1952], p 289
Aortic coarctation: treatment by grafting [1952], p. 290
Aortic coarctation: results of treatment [1952], p 290
Pulmonary stenosis: kymography and catheterization [1952], p. 290
Commissurotomy in mitral stenosis [1952], p 291
Finger-fracture valvuloplasty in mitral stenosis [1952], p. 291
Results of commissurotomy [1952], p. 291
Valvulotomy in mitral valve disease [1953], p 318
Patent ductus arteriosus. diagnosis [1953], p. 318
Patent ductus arteriosus. indication for treatment, technique and results [1953], p. 319

344 VEINS—VARICOSE

Abstract

A simple injection treatment of varicose veins [1951], p. 368

345 VISCEROPTOSIS

No further references

346 VISUAL FIELDS—PERIMETRY AND INTERPRETATION

No further references

347 VITAMINS AND NUTRITION IN RELATION TO SURGERY

No further references

348 VITREOUS—INJURIES AND DISEASES

No further references

349 VOLVULUS

No further references

350 YAWS

Abstract

Antibiotic therapy [1952], p. 292

INDEX

D

E

F

G

INDEX

R

S

T

U

V

W